Is it all necessary?
Defining new protocols of vestibular assessment

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Abstract

Introduction: Scientific evidence is inconclusive about a golden standard to examine peripheral vestibulopathy. A single test has not been found strong enough to be used as reference, while many comparisons between tests are made. A combination of video head impulse testing (vHIT), velocity step testing (VST), bithermal calorics and Dizziness Handicap Inventory (DHI) questionnaire is used in the Radboud University Medical Centre (RadboudUMC). This study tried to find evidence for a golden standard in a large sample of unilateral vestibular patients with a cochlear implant (CI) or vestibular schwannoma (VS). The pediatric vestibular protocol was also examined, because this topic also lacks consistent evidence. A comparison was made between vestibular results pre and post-CI and the protocol was assessed, so that participation of the pediatric patients could be increased.

Method: Two experiments were performed in different age groups. In experiment A, the agreement and correlations were assessed between results of the subjective DHI and objective VST, vHIT and calorics. In an additional analysis, the prediction of vestibular impairment by vestibular test results was assessed. In experiment B, pre and post-CI pediatric vestibular results were compared. The same analyses as in experiment A for a golden standard were tried for the pediatric results. A literature search was also done to assess which questionnaires could be applied in a pediatric protocol. Further adjustments were created based on experiences of other vestibular labs.

Results: The results of experiment A showed that the VST, vHIT and calorics poorly predicted DHI scores, although the difference between impaired and unimpaired patients could be predicted in a statistical model. Parameters of all vestibular tests but VST could predict these differences. In experiment B, no significant differences were found between the pre and post-CI vestibular results of children aged six months to seven years. A predictive model of vestibular dysfunction could not be formed due to the relatively small sample of pediatric patients (N=27). Adjustments for the pediatric protocol were applications for oculomotor testing and the vHIT and by implementing DHI for patient caregivers.

Discussion & conclusion: In experiment A, it was tried to compose an optimal vestibular test battery for patients with unilateral vestibular weakness (UVW). The protocol should contain all used vestibular tests: VST, vHIT, calorics and DHI, due to the fact that every test assesses a different component of the vestibular system. The results showed that objective tests poorly predicted the subjective DHI questionnaire and showed weak correlations between the objective tests. This indicated no redundancy between tests. Although the VST was not included in the model to predict impairment, it is the only test that monitors bilateral vestibular function and compensation abilities. These arguments led to inclusion of the VST in the protocol.

In experiment B, pre and post-CI vestibular results of pediatric patients were assessed on significant changes. Due to the amount of missing data and the small sample size, only indicative conclusions can be drawn. However, no significant differences seem to occur between pre and post-CI assessments in children aged from six months to seven years. Due to the amount of missing data, the second research question, which vestibular tests are redundant in the pediatric protocol, could not be answered. Adjustments for the pediatric vestibular protocol were proposed to use child-friendly materials to test oculomotor function and vHIT and to implement the DHI for patient caregivers.

Recommendations: The vestibular protocol should consist of VST, vHIT, bithermal calorics and DHI. Future research should add the cervical and ocular vestibulo-evoked myogenic potential (cVEMP and oVEMP) tests to assess the otoliths and add a healthy control group to diminish bias in the study. More research should be focused on isolated posterior canal loss in the VS-population. In the pediatric experiment, the sample has to be enlarged. Within subject comparisons also have to be made to control for an age effect. The DHI for patient caregivers has to be validated and norm values have to be formed, before the questionnaire can be implemented completely. This study recommends trying all vestibular tests in pediatric assessments and measuring children pre and post-CI operation.

Contents

Preface

This work is written for the Radboud University Medical Centre and as thesis for my master Speech language pathology of the Radboud University in Nijmegen. I have learned a lot about the vestibular system and the technical ways to assess it during this project. It was very interesting to be part of the scientific research field, the clinical setting and to collaborate with different experts.

Without the help of different people, I could not have done this project. First I would like to thank dr. Andy Beynon, for his counselling and feedback during my project. Another person I am very grateful, is professor Roeland van Hout. He has helped me handle all the data and picking the right analyses. Further I would like to thank Karin Krommenhoek and Jacquelien Jillessen, for sharing their expertise of vestibular assessment with me and helping me become acquainted with the techniques.

Now the project has come to an end, it also means that my period of studying has come to an end. I hope you will read this paper with as much interest as I had during the project.

Kristy Kolmus

Glossary

Caloric testing	Assessment of the vestibular system by irrigating an ear with water of 30 or 44^{0}C, which causes the endolymph to shrink or expand. The vestibular function is stimulated and in this way the responsiveness and symmetry can be compared between the two ears (Desmond, 2011).
Dizziness	The impaired perception of spatial orientation without a false sense of motion (Bisdorff et al., 2009).
Dizziness Handicap Inventory (DHI)	Questionnaire to identify the subjective problems of the vestibular function (Mutlu & Serbetcioglu, 2013).
Electronystagmography (ENG)	Assessment of the eyes on the appearance of a nystagmus by placing sensors near the eyes and registering the action potentials caused by movements of the pupils (Desmond, 2011).
Nystagmus	An appearing eye movement when the vestibular system functions normally. It consists of a slow phase (trying to fixate on a moving object) and a fast phase (return to a point in the visual field; Desmond, 2011).
Optokinetic tracking	Part of the oculomotor tests where a nystagmus is evoked by exposing the patient to fast moving light stripes (Desmond, 2011).
Saccades	Rapid movements of the eye which appear when the eye tries to fixate on an object (Eza-Nuñez, Fariñas-Alvarez & Fernandez, 2016).
Saccule	A part of the membranous labyrinth that responds to static orientation of the head in the vertical plane (Khan & Chang, 2013).
Semicircular canals (SCCs)	Three arches that form the kinetic labyrinth. The posterior, lateral and horizontal ducts are the parts of the membranous labyrinth that detect motion of the head in different angles (Khan & Chang, 2013).
Utricule	A part of the membranous labyrinth that detects the static orientation of the head in the horizontal plane (Khan & Chang, 2013).
Unilateral Vestibular Weakness (UVW)	Vestibular impairment in one ear. Defined in this study as areflexic results on both temperatures of caloric testing and deviant vHIT gains in all three canals.
Velocity step testing (VST)	A type of rotational chair testing. The vestibular system responds to inertia of the endolymph due to rotational forces. Bilateral vestibular function is assessed (Desmond, 2011).
Vertigo	The impaired sensation of self-motion, when one is at rest or during normal movement of the head (Bisdorff et al., 2009).
Vestibulo ocular reflex (VOR)	The response of the eyes when the vestibular system is stimulated during motion of the head. The eyes turn in the opposite direction of the head and are measured by the gain: the ratio of slow phase compensatory eye velocity to head impulse velocity (Alhabib & Saliba, 2017).

Vestibular system	The utricle, saccule and the three semicircular canals. They respond to gravitational forces and movements of the head in different angles (Khan & Chang, 2013).
Video head impulse test (vHIT)	A passive and short test based on the VOR in relation to high-acceleration head movements. The test assesses each semicircular duct separately.

1. Introduction

The vestibular system[1] is one of the six senses people use to function in everyday life. The system heads equilibrium, postural balance and spatial orientation. Many differences exist between the other senses and the vestibular system. The most striking difference is that the vestibular system is a multimodal process and aggregates different modalities, whereas the other senses can function independently (Angelaki & Cullen, 2008). It is influenced by the multisensory interactions from visual, vestibular and somatosensory organs. Thus, signals are caused by fluctuations in vision, gravitational force and muscle tone. They are processed centrally in the brainstem, the cerebellum and the cortex and peripherally in the vestibular system (Khan & Chang, 2013). This thesis focuses on the latter system.

Dizziness or vertigo can be caused by abnormal processing of equilibrium. The difference between the two terms is that vertigo contains a false sense of motion, while dizziness describes a problem in spatial orientation (Bisdorff et al., 2009). These sensations can be spontaneous, triggered or dependent on certain movements. Besides postural balance problems, they can cause vegetative reactions (e.g. nausea or fatigue) or neuropsychiatric symptoms such as anxiety (Bisdorff et al., 2009). So problems with equilibrium can contain different complaints.

In short, the vestibular system is an important organ for equilibrium, postural balance and spatial orientation. When an individual encounters issues in the processing of this system, it can cause a variety of objective and subjective problems. The vestibule can be examined objectively in different ways, to see which part of it is damaged. But consensus about a golden standard of the different tests does not exist in literature. This study will try to find evidence for a standard test battery. Further it is known that vestibular assessment in children is hard and not many articles of pediatric vestibular research are published yet. In addition to finding a golden standard test battery, vestibular results of pediatric patients will be compared pre and post cochlear implantation (CI) and adjustments to the protocol will be assessed.

1.1 Anatomy & physiology of the ear

Because the vestibular system consists of several organs and is part of a greater structure, the relevant anatomy and physiology of the ear will be described first. The ear consists of three different parts. These are the outer ear, the middle ear and the inner ear. The first contains the auricle and the meatus (see figure 1; Seikel, King & Drumright, 2010). The middle ear is separated by the tympanic membrane from the meatus. Attached to this membrane are the auditory ossicles: malleus, incus and stapes. At the end of the chain is the oval window, which induces the fluid in the inner ear. In this part of the ear the vestibular and auditory systems are present. These systems make it possible to hear and to maintain your postural balance. (Dallos, 2012)

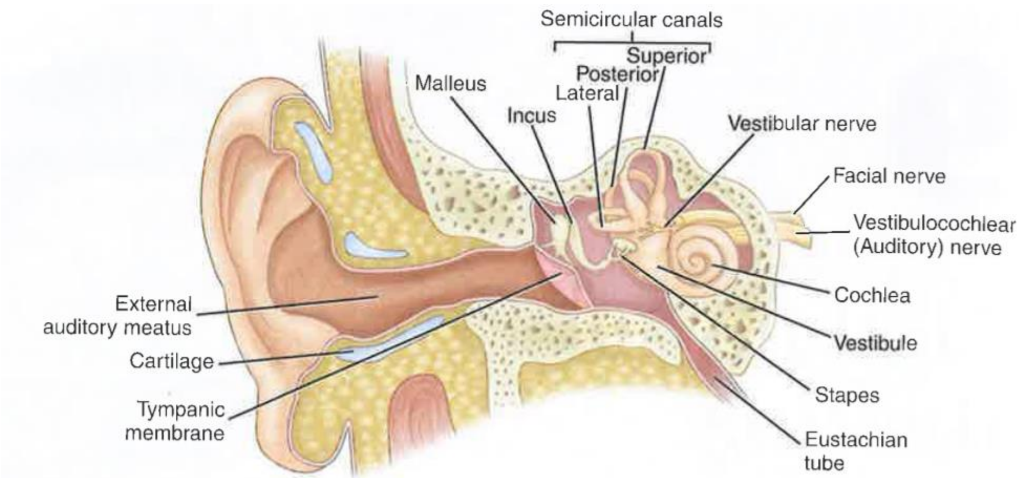


Figure 1. Schematic of frontal section revealing outer, middle and inner ear structures. Reprinted from *Anatomy & Physiology for Speech, Language and Hearing* (p. 448), by J. A. Seikel, 2010, New York, NY: Delmar Cengage Learning. Copyright 2010 by Delmar Cengage Learning.

[1] The key concepts of the vestibular system and its assessment were elucidated in the glossary.

1.1.1 Auditory system

The auditory system in the inner ear is the cochlea, which is subdivided in different compartments such as the scala media. In this part, the organ of Corti is located on the basilar membrane, which contains hair cells who convert mechanical stimuli in action potentials.

The tympanic membrane vibrates by sound waves so that the auditory ossicles start to move the oval window. This stimulates the auditory system in the inner ear, which is a snail-shaped structure and consists of bony and membranous structures. The osseous cochlea is divided into two parts through the spiral lamina and wallows around the central core, the modiolus. The upper compartment of the cochlea is the scala vestibuli and interacts with the oval window, while the lower part is the scala tempani and communicates with the round window. The two compartments are filled with perilymph and are connected by the helicotrema, a membrane in the top of the cochlea. Next to these two scalas is a third compartment, the scala media. It is located in the scala vestibuli on the basilar membrane, which covers the outside of the spiral lamina. This compartment is filled with endolymph and communicates directly with organs of the vestibular system. Within the scala media is the organ of Corti, which is situated on top of the basilar membrane. This membrane is stimulated in its whole, although the greatest deflection of the membrane represents the frequency of the sound. Through the basilar membrane, nerve fibres are connected to hair cells (stereocilia) in the organ of Corti. These hair cells move induced by the endolymph and convert these mechanical stimuli in action potentials. These electrical stimuli can be processed in the auditory regions in the brain. (Dallos, 2012)

1.1.2 Vestibular system

The peripheral vestibular system is situated next to the auditory system in the bony labyrinth of the inner ear. The parts of this labyrinth are the cochlea, the vestibule and the three semicircular canals (SCCs; Desmond, 2011). The vestibular system is situated in the latter two parts. Within these two structures, the membranous labyrinth is located. This labyrinth consists of five different organs: the saccule, utricle and three SCCs (see figure 2; Siegel et al., 2010). They detect head motion and gravitational forces on the body in different angles. These membranous organs are surrounded by perilymph and filled with endolymph (Khan & Chang, 2013).

The otolith organs, the saccule and the utricle, are located in the vestibule. These organs detect static orientations. They are activated by linear acceleration, gravitational forces and tilting of the head (Khan & Chang, 2013). The sensory parts of the utricle and saccule are called maculae. The utricle responds to horizontal motions, whereas the saccule senses vertical motions (Desmond, 2011). In the gelatinous membrane of the maculae are hair cells, which contain a longer cell (the kinocilium) and several shorter ones (the stereocilia). On top of this membrane are small calcium carbonate particles located, called the otoconia or otoliths. When gravitational forces or movements of the head are performed, these otoconia move so that the hair cells are stimulated (Khan & Chang, 2013). In this way linear accelerations are processed by the utricle and the saccule in the horizontal and vertical planes.

The other vestibular organs are situated in the SCCs. They pertain the kinetic labyrinth, which entails that they do not respond to static positions, while the otolith organs do. The superior and posterior SCCs are situated in an angle of 45 degrees in the sagittal plane and the lateral SCCs are aligned in an angle of 30 degrees in the axial plane (Khan & Chang, 2013). So in pairs the contralateral SCCs form a three dimensional vector representation of rotational acceleration. In the SCCs flows endolymph which activates the crista ampullaris in each SCC. This is a sensory neuroepithelium covered by a gelatinous substance, embedded in hair cells and located in a delated area, the ampulla (Desmond, 2011). The hair cells respond to bending of the cupula in the opposite direction of the rotation. Excitation of hair cells in one SCC, will diminish excitation in the contralateral SCC (Khan & Chang, 2013). Because of these three SCCs in each ear, it is possible to detect head movements and maintain equilibrium.

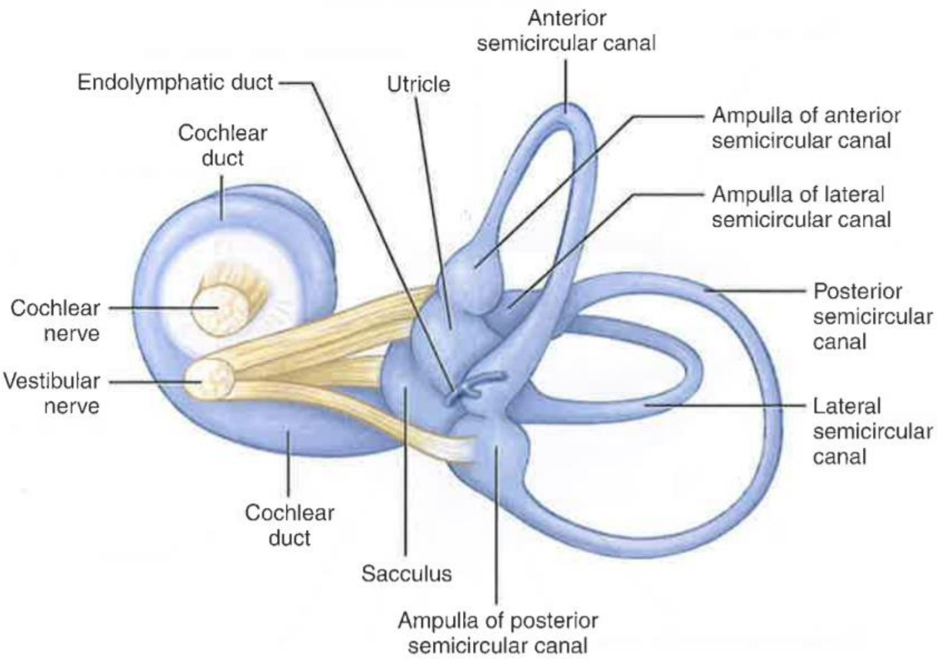


Figure 2. A schematic of relationship of vestibule, semicircular canals and cochlea. Reprinted from *Anatomy & Physiology for Speech, Language and Hearing* (p. 463), by J. A. Seikel, 2010, New York, NY: Delmar Cengage Learning. Copyright 2010 by Delmar Cengage Learning.

Pathology

In the complex structures of the auditory and vestibular system, many different problems can occur affecting hearing and equilibrium. The most common vestibular deviations are discussed briefly.

The most frequent vestibular disorder is the Benign Paroxysmal Positional Vertigo (BPPV) and it accounts for 25% of the vestibular patients (Desmond, 2011). It causes episodic vertigo, because the otoconia are detached from their place and stimulate the SCCs instead of the utricle (Solomon, Kim & Zee, 2014). The vertiginous episodes last intense for one minute and less intense for several hours until a day. The disorder can be treated with certain head manoeuvres, which relocate the otoconia (Solomon et al., 2014). Another common vestibular disorder is vestibular neuritis. It is thought to be caused by a viral inflammation of the vestibular nerve, which results in a sudden onset of vertigo lasting for approximately 24 hours. All five vestibular organs can respond to the inflammation and cause vegetative reactions (Desmond, 2011). Furthermore, there is Meniere's disease, which impairs the inner ear and results in unilateral diminished hearing, tinnitus, aural fullness and episodes of vertigo (Patel & Isildak, 2016). The hearing does not recover entirely most of the times after an attack, but is mostly affected during the episodic vertigo that can last 20 minutes up to several hours. The origin of the disease is thought to be in the process of endolymph regulation, called endolymphatic hydrops (Patel & Isildak, 2016).

In this study, only pathologies with chronic vestibular deficits are examined. These are caused by a vestibular schwannoma or CI-surgery. A vestibular schwannoma (VS) implies a slow growing, benign tumour encapsulated in the cerebellopontine angle. It affects the hearing unilaterally, can cause tinnitus and gradually decreases vestibular function (Von Kirschbaum & Gürkov, 2016). Besides internal causes of vestibular impairments, vertiginous problems can also arise when a cochlear implant (CI) is placed in the inner ear. During the surgery, an electrode is inserted in the cochlea to improve hearing (Chen et al., 2016). This can impair the endolymph regulation, which can result in vestibular impairment (Thierry et al., 2008).

1.2 Vestibular assessment

The assessment of the vestibule is based on different functional levels and structures in the system. The diagnostic assessments are measured by particular eye movements, which are responses to vestibular stimuli. The different tests and the corresponding reactions of the eyes are characterized further below and in addition to the objective tests, a questionnaire is described for the subjective vestibular problems.

1.2.1 Video head impulse test (vHIT)

The test assesses the vestibulo ocular reflex (VOR) in relation to unpredictable and fast head movements in a maximum angle of 20 degrees. Each of the SCCs can be tested individually by this test (Alhabib & Saliba, 2017). The protocol is relatively simple for the patient and it only takes several minutes to complete. The head is rotated and the VOR makes it possible to maintain a stable image of the visual field (Khan & Chang, 2013). The outcome measure of the VOR for each SCC is the gain, which is characterized as the ratio of slow phase compensatory eye velocity to head impulse velocity. So the vHIT is a passive and short test, which assesses the function of each SCC separately.

1.2.2. Electronystagmography (ENG)

Another way to examine the vestibular system, is by electronystagmography (ENG). Movements of the pupils are detected by sensors as corneo-retinal action potentials. The signals are registered by a computer and can be interpreted by the clinician (Desmond, 2011). This part of the vestibular assessment consists of different tests.

Oculomotor tests

The assessment is initiated by calibration of several eye movements. Oculomotor testing consists of saccadic tracking, smooth pursuit tracking, optokinetic tracking, spontaneous nystagmus and gaze-evoked nystagmus (Wuyts, Furman, Vanspauwen & Van de Heyning, 2007). During these tests the central pathways of the cerebellum are tested and abnormalities can be seen as signs of potential neurologic disorders (Desmond, 2011). If no abnormalities are registered, the assessment of vestibular responses will be started.

The saccades are the first assessed eye movements. These are rapid, voluntary and reflexive eye movements which try to fixate the eyes accurately on a new object (Desmond, 2011). If there is a constant delay of 260 milliseconds or more, the saccades will be considered deviant. The next eye movement is the smoot pursuit. It is used to maintain fixated gaze on moving objects. The movement is assessed on symmetry of the eye deflections and the gain of the eye velocity in relation to the target velocity (Desmond, 2011). Both parameters will be perfect when the ratios approach the number one. This indicates that the deflections are the same and the velocities are similar. Another part of the oculomotor tests is the optokinetic tracking. During this test the optokinetic nystagmus is evoked by showing the patient repetitive moving visual stimuli (Desmond, 2011). A nystagmus appears, because the patient tries to follow each stimulus a short period (the slow phase) and then returns to the centre (the fast/saccadic phase; Desmond, 2011). This movement, the nystagmus, normally appears when the vestibular function is stimulated.

In addition to the calibration movements, the eyes of the patient are also assessed on the appearance of a nystagmus. This is assessed spontaneous or triggered in gaze (Wuyts et al., 2007). The causes of the nystagmus can be various and can originate peripherally or centrally. An innocent form is the infantile idiopathic nystagmus, where no underlying neurological problems or eye conditions are present (Hussain, 2016). The appearance of a nystagmus in these tests can interfere with the interpretation of latter vestibular assessment (Wuyts et al., 2007). By assessing these eye movements it can be concluded that no abnormalities are present for measurement of the vestibular system.

Velocity Step Testing (VST)

After calibration of the eye movements, the rotary chair testing is performed. During rotation both vestibular systems are stimulated horizontally and a nystagmus appears due to inertia of the endolymph. When the endolymph rotates in the same speed as the chair, the eye movement diminishes. Based on symmetry, the velocity of the slow phase and the gain of the nystagmus will be assessed if there is hyporeflexia, hyperreflexia, normal vestibular function or areflexia (Wuyts et al., 2007). A time constant is also registered as indication of decreasing nystagmus velocity and asymmetry between both ears (Desmond, 2011). In this way the vestibular system is assessed bilaterally.

Bithermal caloric testing

During the last objective test, the vestibular response of each ear can be assessed. This entails caloric testing with two different temperatures. Because of the location of the vestibular system and the reach of the temperature, only the horizontal SCC is provoked (Wuyts et al., 2007). Warm water causes the endolymph to expand so that the vestibular function is stimulated (Desmond, 2011). This causes a nystagmus in the direction of the irrigated ear. Cold water causes a nystagmus in the opposite direction (Desmond, 2011). An abnormal reaction could be a weak or absent nystagmus or a lack of fixation when a visual stimulus is shown (Desmond, 2011).

1.2.3 Self-report measures

In addition to the objective tests, perceived vestibular problems can be assessed by submitting questionnaires. As stated earlier, the vestibular system is multimodal and bilateral of nature. So abnormalities in the objective measurements do not implicate that the patient experiences problems. This can be circumvented by compensation of the vestibular system (Dieterich & Brandt, 2015). Thus, it is also important to identify the experienced problems. The most common questionnaire is the Dizziness Handicap Inventory (DHI). It is a self-reported, validated questionnaire, consisting of 25 items and designed to identify functional, emotional and physical factors associated with dizziness and vertigo (Mutlu & Serbetcioglu, 2013). The Dutch translation is as consistent as the original questionnaire (Vereeck et al., 2009). Besides this questionnaire, more subjective measurements are available such as the Activities-Specific Balance Confidence Scale (ABC), the Falls Efficacy Scale-International (FES-I), the Vestibular Activities and Participation questionnaire (VAP) and the Global Rating of Change Scale (GROC; Friscia et al., 2014). These self-report measures are discussed in this thesis among others so that their implementation can be considered in addition to the current measurements.

1.2.4 Combination of vestibular assessments

To conclude, there are several ways to detect peripheral vestibular dysfunction. A complementary combination is used in the Radboud University Medical Centre (RadboudUMC), which pertains the vHIT, VST, caloric testing and DHI. It enables clinicians to assess the vestibular system of each ear, unilaterally and bilaterally on different levels. Other tests that assess peripheral vestibular functioning are the vestibular evoked myogenic potential tests (VEMPs), positional or positioning tests and posturography. These tests are not part of the protocol of peripheral vestibular assessment in the RadboudUMC and are disregarded for this study.

1.3 Correlations of the vestibular assessment results

Evidence between articles is inconsistent about a golden standard to examine vestibulopathy peripherally. A single test has not been found strong enough to be used as reference, while many different combinations and comparisons are made between studies. In a study that examined the best combination of vestibular tests in 200 patients with peripheral vestibulopathy was found that the best predictive capabilities came from the combination of calorics and rotational chair testing. The authors pointed caloric testing out as most sensitive test in this combination (Ahmed et al., 2009). This test combination was also preferred in the study of Maes et al. (2011). It was examined in 77 patients with unilateral vestibular impairment and 80 healthy controls. Next to calorics and the rotational chair testing, they recommended adding the cVEMP to the test battery due to better specificity than the other tests. However, a more recent systematic review recommends a case-to-case strategy for CI-patients and does not prefer an overall protocol (Abouzayd et al., 2017). There were sixteen studies included in their review and only eight in their meta-analysis. The review revealed that the vestibular tests examine different parts of the system and no test could be recommended as reference test due to a lack of sensitivity. Only calorics, HIT and cVEMP were included in the analysis. These studies showed that comparing evidence between studies is difficult, because they compare different test combinations and use a variety of subjects. However, it seems that calorics is the most validated test, but consensus about which tests should be performed additionally does not exist.

A fairly new test is the vHIT, which is compared to caloric testing in 69 patients with vestibular schwannoma in the study of Blödow et al. (2015). They reported that the horizontal VOR was affected by tumour size in calorics, while it was not in the vHIT. This entailed a moderate correlation between the test results ($r=.54$, $p<.05$). In general however, the caloric tests were more sensitive for a deviant horizontal VOR function than the vHIT (72% vs. 44%). But the difference in frequency examination of the tests pertained that both tests had to be performed to be able to detect problems of the horizontal VOR in the whole frequency range. This meant that the calorics and the VHIT were complementary, instead of redundant (Blödow et al., 2015). Another study agreed with this statement. Eza-Nuñez, Fariñas-Alvarez & Fernandez (2016) compared the vHIT to calorics and rotational chair testing in 115 patients with moderate dizziness complaints, which were measured by the DHI. They observed that the agreement between the tests was low in assessing the horizontal SCCs, although the vHIT seemed the best test for a first impression of the vestibular system. This evidence states that the vHIT is a relevant addition to caloric testing, but cannot replace it.

Besides the objective tests, the DHI questionnaire can be considered for implementation in the standard test battery of vestibular assessment. In the study of Batuecas-Caletrio et al. (2015a), the DHI score was compared to vHIT and caloric results in 30 patients pre and post CI-surgery. One third of the patients had deviant vHIT gains post operatively and showed diminished responses in caloric tests in comparison to before. These patients also showed higher results in the DHI, although the changes were not correlated to the degree of impairment. This resulted in a poor correlation of DHI score and results of the vHIT or calorics. This is in accordance with their former study where 49 VS-patients were followed up for at least a year (Batuecas-Caletrio et al., 2013). In this study was reported that unilateral vestibular impairment resulted in higher DHI scores, but that these results still correlated poorly. Another study confirmed the modest correlation between calorics and vHIT and the fact that the tests are complementary as stated earlier in Blödow et al. (2015). They compared calorics, vHIT and DHI in 30 VS-patients (Tranter-Entwistle et al., 2016). The same conclusions were drawn in the study of McCaslin et al. (2014), in which 115 patients with dizziness symptoms were assessed. In this study was observed that the calorics and vHIT poorly predicted DHI scores or tumour size. The authors concluded that as a result of these weak correlations, the tests had limited diagnostic abilities on their own (Tranter-Entwistle et al., 2016). Because of the bad correlations, implementing the DHI into the test battery of vestibular assessment seems to be relevant.

Different test combinations were compared in studies to assess peripheral vestibulopathy and in combination with different patient groups, it is difficult to compare evidence. The most validated tests are the calorics and the vHIT. The DHI seems a helpful addition as well as the rotary chair testing and the cVEMP, but evidence for a combination of a golden test battery of these tests is not consistent.

1.3.1 Unilateral vestibular dysfunction

Depending on the underlying pathology, the outcomes of the peripheral vestibular assessments can be various. This thesis focussed on the unilateral vestibular weakness (UVW) and for that reason assessed correlations of vestibular tests in patients with VS and CI, although even between these two pathologies differences exist in vestibular symptoms. However, both pathologies can result in chronic UVW. The biggest distinction between subjects with VS or CI is that compensation of VS vestibulopathy can arise effectively, while for CI the symptoms are experienced more. The reason for this is that the vestibular function is affected gradually by the VS, whereas the CI surgery does suddenly (Thierry et al., 2008; Von Kirschbaum & Gürkov, 2016). This study assessed whether the test results differed between patients.

Incidence of vestibular dysfunction due to cochlear implantation varies between 0.33-75%, but a more specific average seems to be 32% (Enticott et al., 2006; Katsiari et al., 2013). In caloric testing for instance, 37% of the 439 subjects with normal vestibular function demonstrated a diminished response (Kuang, Haversat & Michaelides, 2015). This is in accordance with the recent study of Stultiens (2017), where 37.4% of 192 CI-patients deteriorated in caloric response. A higher incidence was reported in the study of Robard et al. (2015) who reported a significant decrease of caloric response in 21 of 29 CI-patients. This high percentage (72.4%) can be due to the small sample size. This diminished caloric response was observed in both ears in another study in 86 patients, altough in less extent in the non-implanted ear (Buchman et al., 2004). No reason was given for this bilateral diminished response. However, it did not have its effect on the self-reported vertigo or postural imbalance. This latter statement is further supported by Krause et al. (2010), who assessed 32 CI-patients with caloric and VEMP testing. They did not find a correlation between diminished vestibular function and vertigo symptoms as well. Besides the incidence of vestibulopathy after CI, demographic factors in relation to vestibular problems were assessed for CI patients. This resulted mainly in non-predictive factors like age, sex, pathology, implanted side, implant type, surgeon, preoperative vestibular function results or symptoms and postoperative vertigo reports (Eticott et al., 2006; Katsiari et al., 2013; Krause et al., 2010; Thierry et al., 2008).

Determining the incidence of vestibulopathy in VS-patients is harder, due to effective compensation of vestibular problems. A clinical group in which this possibly happened, is described in the study of Teggi et al. (2014) for example. In this study only 40% of the 64 subjects with VS reported experiences of imbalance, while 86% were considered to have abnormal vestibular test results (Teggi et al., 2014). In contrast to these assumptions, Batuecas-Caletrio et al. (2015b) found that tumour size is associated with the diminishing vestibular function. This is also confirmed in the study of Day et al. (2009), where 44 VS-patients were tested with VEMP and caloric tests. This correlation applied in particular to larger tumours. Another demographic factor that was assessed is the location of the VS. Results from caloric testing or VEMPs could predict which nerve fibre from the vestibular nerve was affected by the tumour. The VOR during caloric testing, can indicate problems in the superior vestibular nerve to the upper brainstem. While VEMPs assess another reflex, which is innervated by the lower brainstem and affects the inferior vestibular nerve (Day et al., 2009). The review article of Von Kirschbaum & Gürkov (2016) discussed this item also. They concluded that one study validated this line of thinking and the other contradicted it (Borgmann, Lenarz & Lenarz, 2011; Ushio et al., 2009).

The adult subjects of this thesis are patients with CI and VS. In conclusion, their pathologies have different effects on the vestibular function and this results in varying experienced vestibular problems. This study assessed whether their vestibular results differed significantly.

1.4 Differences between the assessments of adults and children

Vestibular assessment in children is challenging due to practical issues like concentration capabilities and instruction limitations. This is shown in the study of Thierry et al. (2015), where only 43 of the 577 unilateral CI implanted children were fully tested post CI-surgery with the HIT, bithermal caloric tests and the VEMP. Only twelve children were assessed both pre and post CI (Thierry et al., 2015). Half had the same vestibular results post CI, four of them had improved results and the other two showed a diminished response (Thierry et al., 2015). The incidence of vestibular dysfunction after CI surgery in children was assessed in a larger sample (N=224) and seemed to be the same as in adult patients, which was about a third of the patients (Jacot et al., 2009). In the CI candidate group only half of the 224 children had normal symmetrical vestibular function, whereas the other half had abnormal caloric responses and 45% had abnormal otolith responses (Jacot et al., 2009). Equal percentages were found post CI-surgery in the study of Thierry et al. (2015), where also 50% of the 43 children had normal vestibular function. In a comparison of children with or without CI, the study of Cushing et al. (2013) found the same incidence of vestibular dysfunction in the children with CI. Furthermore, a third of their 153 implanted children had such severe losses, that it correlated with balance functional problems. In contrast, no correlation was found in the study of Jacot et al. (2009) between vestibular malformation or cause of hearing loss and vestibular function in children. After surgery 30% of the 89 implanted children scored deviant on the vestibular assessments, although only the children with complete areflexia experienced problems (approximately 10%; Jacot et al., 2009). The authors explained this by the fast compensation abilities of children of sensory deficits (Jacot et al., 2009). They concluded that vestibular assessment needs to be done before and after the CI surgery, to keep track of the changes in vestibular function (Jacot et al., 2009). The study of Cushing et al. (2013) describes this need also.

The vHIT is a relatively new method and has proven its use and accuracy (MacDougall et al., 2012). The study of Hamilton, Zhou & Brodsky (2015) showed the effectiveness of the test for examination of the lateral ducts in children. They tested 26 children with vestibular dysfunction and 23% scored an abnormal lateral function. The vHIT gain correlated significantly with the lateral duct function, but the vHIT results were more sensitive than the rotary chair testing results (Hamilton et al., 2015). In the study of Nassif et al. (2016), 16 children with a CI and 20 normal hearing children (NH) were compared on lateral VOR by the vHIT. In addition to the former study, no significant differences were found between the groups in the non-implanted ears (M_{gain} CI group=.93, M_{gain} NH group=.89, p=.2). No significant difference was found between the implanted and contralateral ear in unilateral implanted children (t=1.32, p=.2). In the whole sample, they also tested the lateral VOR gain turning the CI on and off. No significant difference between unilateral or bilateral implantation was found (F(1, 36)=.07, p=.8), while CI status showed a significant effect (F(1, 36)=6.63, p=.01). This resulted in higher gains when the CI was turned on in both unilateral and bilateral implanted children. So these studies showed that the vHIT is a useful addition for pediatric vestibular assessment.

Another study that supports the need of insight in vestibular function of children with CI, is the one of Wolter et al. (2015). They examined the incidence of vestibulopathy in children with CI failure due to falling. They found in 22 children that absence of bilateral horizontal canal function enlarged the odds of CI failure by almost eight times. This is important for clinicians to add to their advice to parents in the treatment of their children. Not only can vestibulopathy result in CI failure, but also in a delayed motor development. In the article of Inoue et al. (2013) is shown that children with bilateral vestibular dysfunction acquired head control and independent walking in a later age than children with normal vestibular function. The first ability was delayed more than five months in 30% of the children and independent walking was delayed over 18 months in 26% of the 76 children (Inoue et al., 2013). However, in a particular age group no significant difference was found in vestibular function before and after CI-surgery measured by caloric tests, HIT and VEMPs (Ajalloueyan et al., 2017). They assessed 27 children in the age of one to four years old. So they conclude that for this age group, CI does not affect vestibular function.

Only a few studies have compared age-related complications of CI between adult and pediatric populations (Farinetti et al., 2014; Hansen et al., 2010). In the study of Farinetti et al. (2014) 235 children were compared with 168 adults after CI surgery. They found that in 14.9% of the entire population a minor complication arose, whereas in 5% of the patients a major complication was found. This was in accordance with incidences found in earlier studies, where it varied between 9-39% depending on the definitions and inclusion of complications (Hansen et al., 2010). Minor complications after CI surgery were infections like acute otitis media or infections of the skin, tinnitus in the implanted ear, temporary vestibular dysfunction and neurological complications as facial nerve palsy. In a global comparison, a significant difference was found between the adult and pediatric population, which meant that adults (26.8%) had more complications than children (10.2%, p=0.002; Farinetti et al., 2014). This was also seen in minor complications, where adults had problems in 21.4% of the cases in comparison to 10.2% of the children (p=0.002). For the major complications, no significant difference was found between the age groups (Farinetti et al., 2014). However, in the study of Hansen et al. (2010) vertigo was the most common complication found after CI surgery in 367 patients (25% in adults and 2.2% of the children), despite the fact that these complaints were only temporary and were resolved one month after surgery. For this latter reason, Hansen et al. (2010) calculated incidence with and without vestibular dysfunction. So vestibular dysfunction is only seen as a minor but common complication after CI surgery, due to the temporary nature of the experienced problems.

To summarize, vestibular assessments are challenging for both the children and the clinician. Evidence states that adults acquire more complications post CI-surgery than children do. The vestibular dysfunction is one of the most common complications, although it is only experienced temporary. Due to this fact, vestibular dysfunction is not seen as a complication in some articles and is left out of analysis due to the compensation abilities. This limits determining incidence of vestibulopathy in pediatric patients.

1.5 Aim of the study

The aim of this study was to examine the current protocols of the vestibular assessment in the RadboudUMC. There is no consensus in the scientific field about a standard test battery that should be used for a vestibular protocol. The aim of this study was to find evidence for such a protocol of the vestibular assessment. This was done in two experiments, where different age groups were examined.

The first experiment was aimed at adult patients. To our knowledge, no articles were published yet that were focussed on the necessity of vestibular tests of patients with UVW due to VS or CI. The aim of this experiment was to find evidence for a protocol for these patients by data analyses of a large sample. In this way would be assessed whether there were any vestibular test combinations that could predict vestibular function after CI surgery or VS growth. Furthermore, subjective vestibular problems were linked to objective vestibular test results by correlating DHI scores with VST, vHIT and caloric results to assess whether objective vestibulopathy correlated with experienced balance problems.

In the second experiment the data of the pediatric population pre and post CI-surgery were analysed to see whether significant differences between the test results existed. In addition to these differences, correlations between tests were examined. Furthermore, experience was gained in the vestibular assessments for both adults and children to unveil difficulties in the pediatric assessment and new implementations could be tested to improve participation of the children. For instance, no subjective questionnaires were used in vestibular assessment for children in the RadboudUMC. A few options were translated and considered for implementation.

Thus, in this study theoretical and practical lines of research were combined. The main part of the study was retrospective data-analysis, which was supplemented with a practical approach of new implementations. Because of the differences in age groups, two experiments and multiple research questions were formed.

1.5.1 Research questions

Experiment A – agreement of test results in adult patients with VS or CI

Main question 1

Which objective vestibular function test results agree with the DHI score in adult patients with CI or VS?

Main question 2

Which vestibular assessments are redundant in adult patients with CI or VS?

Experiment B – pre/post comparison of pediatric patients with CI

Main question 1

Which results within de objective vestibular assessment differ pre and post CI-surgery in pediatric patients with CI?

Main question 2

Which results within the vestibular assessment are redundant in pre and post-CI vestibular assessments of pediatric patients?

Sub question 1

In which ways can the vestibular assessment of young children (age 0-6 years) be improved?

2. Method

Two experiments were formed with several questions due to the different age groups. The methodology of these experiments were described in the data collection, while the sub question of experiment B was outlined last.

2.1 Data collection

To answer the research questions, the different tests that were performed at the RadboudUMC and their outcome measures of vestibular assessment were assessed. These tests were the video head impulse test (vHIT), the bithermal caloric tests, the velocity step test (VST) and the Dizziness Handicap Inventory (DHI; see table 1).

Table 1. Outcome measures per vestibular test

Test	Outcome measures
vHIT	VOR gain per semicircular canal (SCC)
VST	Time duration, velocity, gesamtamplitude (GA) per direction
Caloric test	Maximum slow phase velocity (MSPV) per side and per temperature
DHI	Total and sub scores (physical, functional, emotional)

The outcome measures were all numeric variables, which were suited for statistical analysis. They were also converted into ordinal or nominal variables to indicate deviant values.

2.1.1 Experiment A: correlations in test results of adult patients with UVW

To examine the agreement between the objective tests and the DHI, a sample of patients with unilateral vestibular dysfunction was collected in a database.

Subjects

The data included in the analyses, was retrieved from a large sample of patients. A study was performed in 2017 to compare vestibular test results pre and post cochlear implantation (CI; N=201; Stultiens, 2017). The data of this study was partly included in this study and complemented with data of patients with a vestibular schwannoma (VS). The inclusion criteria for the subjects in this experiment were:

Inclusion criteria

1. The age of the patient was seven years or more at the time of testing[2];
2. The patient was diagnosed with VS or implanted with CI unilaterally;
3. The CI patient has been assessed pre- and post-CI surgery;
4. A combination of the following vestibular tests was performed: vHIT, caloric tests, VST or DHI;
5. The patient has been tested in the period of May 2013 until April 2017.

Exclusion criteria

1. Besides VS or CI, the patient has been diagnosed with other pathologies;
2. The patient was diagnosed with bilateral VS;
3. Caloric testing was performed using air stimulation.

Statistical analysis

To analyse the data, IBM SPSS Statistics Version 22.0.0.1 was used (IBM Corp. Released, 2013). Patient characteristics were described for the adult patients by running descriptive statistics. To answer the research questions, different steps of analyses were taken. In the first step was assessed whether the tests could differentiate accurately between impaired and unimpaired patients and whether CI and VS-patients had significantly different results on the tests. A vestibular system would be considered impaired if the patient had a deviant gain on all three canals of the vHIT and an areflexic result of both

[2] The age limit is set at seven years, because the RadboudUMC uses the pediatric protocol until that age. Older children are assessed in the adult vestibular protocol.

warm and cold calorics. The latter was defined as a maximum slow phase velocity (MSPV) below five on both warm and cold calorics, while the first had different limits for each duct: anterior gain <.74, lateral gain <.81, posterior gain <.78 (Murnane et al., 2014). Independent t-tests, χ^2-tests or ANOVA's were carried out to examine differences between the impaired and the unimpaired group and between the VS- and CI-group. These analyses showed whether tests differentiated correctly between impaired and unimpaired patients and whether the CI and VS-patients could be pooled for further analyes. For the t-tests the assumption of normality was checked by the Kolmogorov-Smirnov test. If this test was significant, the assumption would still not be violated, due to the amount of subjects used in this experiment. For the χ^2-tests, the following assumptions were checked: all variables were categorical, no expected values were zero and no expected values were below five. For the ANOVA's was checked for homogeneity of variance in the Levene's test. If this test was significant, it would be corrected by calculating F_{max}. To examine if parts of the vestibular tests correlated within a test, Pearson's correlation tests would be performed. For this analysis, the data was checked on continuous variables, related pairs, absence of outliers, linearity and homoscedascity. The labels for correlation strength were: r=0.00-.60 weak, r=.60-.80 moderate, r=.80-1.00 strong (Field, 2009). The same categories were assumed for η^2.

In the second step, correlations and three models were analysed to answer the research questions. It was expected that no agreement existed between the results of the objective vestibular tests and the DHI score. No overlap was suspected between the objective vestibular tests, which would indicate no redundancy. To test these hypotheses, the correlations between the different vestibular assessments were analysed by performing Pearson's correlation coefficient tests. The variables were checked for the same assumptions as mentioned earlier and the same correlation strengths were assumed.

To answer the first research question, a predictive model was formed in a linear regression to examine whether the parameters of the VST, calorics and vHIT could predict the DHI total score (model 1). The relationship of the dependent and independent variables was checked in scatterplots for linearity and in the Kolmogorov-Smirnov test on multivariate normality. The data was also tested on multicollinearity by the Variance Inflation Factor (VIF), which needed to be less than ten to not violate the assumption. The last assumption for the logistic regression was homoscedasticity, which was checked in a scatterplot of residuals. A second model was analysed in a multinomial logistic regression to assess if the same parameters could predict categories of the total DHI score (mild, moderate, severe; model 2). Before this analysis was run, six assumptions were checked: 1) the dependent variable was measured at the nominal level, 2) independent variables were continuous, ordinal or nominal variables, 3) the observations were independent, 4) no multicollinearity was found in the data (checked with VIF), 5) a linear relationship existed between a continuous independent variable and the logit transformation of the dependent variable and 6) no outliers were shown in the data.

To answer the second research question, whether redundancy exists between tests, a third model was analysed in a logistic regression (model 3). This analysis assessed whether all vestibular tests (VST, calorics, vHIT and DHI) could predict which patients were considered to be impaired and which were unimpaired. For this analysis the dependent variable had to be binary and coded correctly (0=unimpaired; 1=impaired). Another assumption recommended a stepwise method to maintain a good fit of the model. The last assumptions required a large sample size and linearity of the independent variables with the log odds.

2.1.1 Experiment B: pre/post comparison of pediatric patients with a CI

To answer the main questions of this experiment, a comparison was made to see whether pre and post CI-surgery vestibular results were different in pediatric patients. Additionally, the same analyses as in experiment A would be run in this sample to determine if in the protocol of the pediatric assessment also used redundant tests.

Subjects

The subjects were the pediatric patients with CI. The inclusion and exclusion criteria for this experiment were:

Inclusion criteria

1. The patient was less than seven years old at the time of testing;
2. The patient has been implanted with CI unilaterally or bilaterally;
3. The patient has been assessed pre- and post-CI surgery;
4. At least one of the following vestibular tests is performed: vHIT, caloric tests or VST;
5. The patient has been tested in the period of May 2013 until April 2017.

Exclusion criteria

1. The results of the VST and caloric tests are not reliable due to a low amount of nystagmus beats (<6);
2. The patient has been diagnosed with other pathologies, besides their CI.

Statistical analysis

Before the statistical analyses were performed, the patient characteristics were described by running descriptive statistics. Furthermore, success rates were calculated for each vestibular test. A test would be considered successful if the results were reliable and useful. A failed test had little to no results or these could not be considered reliable. To answer the research questions, hypotheses were formed. First, significant differences were suspected between the vestibular results of the two assessments due to the CI-surgery. Second, no correlations were expected between the tests. To test these hypotheses, the correlations and interactions between the different results were examined. To test the assumptions, Levene's test was run and if necessary F_{max} was calculated for correction of normality. Dependent t-tests were run to see whether there existed significant differences in the test results pre and post CI-surgery. Secondly the correlations between the different vestibular assessments were assessed by performing Pearson's correlation coefficient tests. For this analysis, the data was checked on continuous variables, related pairs, absence of outliers, linearity and homoscedascity. To assess redundancy in test of the pediatric protocol, the same logistic regression as in experiment A would be applied in this experiment. The same assumptions were checked for this analysis.

Improvements of the pediatric vestibular assessment

Following the results of the data analyses, adjustments to the protocol can be made. As stated earlier, performing the vestibular assessments in children is challenging due to several reasons. This can be caused by limitations of instructions, concentration capabilities or fatigue. The research lab and different tests could be adjusted to make them more attractive to children. But before adjustments of the assessments could be made, experience of the vestibular assessments was gained with both adults and children. The protocol of the tests is outlined further below of the vHIT, ENG and the DHI.

Video head impulse test

During the vHIT, the patient sits in front of an infrared camera without goggles. A Synapsys Ulmer camera is connected with a computer with software from the same manufacturer (Synapsys, 2014). The patient is asked to look at three different dots on the facing wall: one right ahead and the other two in angles of 20 degrees in the horizontal plane from the first dot. The camera detects the pupils of the eye so that it can register the eye movements. The patient is asked to fixate on one dot, when the head is accelerated by the hands of the clinician. Dependent on which dot, a combination of SCCs can be assessed with a certain head movement (Alhabib & Saliba, 2017). Both horizontal SCCs are examined with an acceleration between 20 degrees left and right. The clinician has to accelerate the head in a plane with a velocity of $1500\text{-}2000^0/s^2$. The computer determines whether the movement and acceleration are correct and whether the response of the eyes is normal or deviant. When six movements of every SCC are accepted, the computer is able to determine whether it functions normally. This is based on the VOR gain, which is different for each SCC. In the normative study of the SYNAPSYS Ulmer device, the norm gains were .74 for the anterior SCC, .81 for the lateral SCC and .78 for the posterior SCC (Murnane et al., 2014).

Electronystagmography

Not only can the vestibular system be assessed by head movements, but also by temperature change and rotational forces. Instead of a camera, electronystagmography (ENG) is used. During the assessment the patient sits in a rotational chair and nine surface electrodes are placed on his head.

Two in the vertical plane and two in the horizontal plane and the last sensor is placed on the forehead as reference. Before these sensors are placed, the skin is cleaned with alcohol and scrubbed a little to diminish impedance.

When everything is set, the calibration movements can be performed in the dark. The patient sits in the rotational chair and is asked to follow a light dot with the eyes. The head needs to be still. For the saccades, the dot jumps between fixed places in the horizontal and vertical plane and this is repeated at random in the horizontal plane. The movements are judged based on the velocity and accuracy. During smooth pursuit the dot moves from 10 degrees left to 10 degrees right and back several times. This movement is judged on the same parameters as saccades. In the optokinetic tracking the patient is asked to look at moving stripes and to fixate on one of the two colours. The stripes move in different speeds, which mimics velocities of a nystagmus. Both directions are assessed and will indicate if the patient is able to show a nystagmus when the vestibular system is stimulated. The last calibration is done to look at a spontaneous or gaze-evoked nystagmus. If a nystagmus appears during fixation or without, it will be corrected in the other assessments.

Velocity step testing

During this test the patient sits in a Jaeger Toennies rotational chair in the complete dark and rotates to the right in a maximum velocity of 0.25 Hz. Software BalanceLab (BLAB0-171-AA-02) is used. At the start of the rotation, a nystagmus appears due to inertia of the endolymph and when the endolymph rotates in the same velocity of the chair it diminishes again. After 90 seconds, the chair suddenly stops and the endolymph continues to rotate so that the nystagmus appears again. After a couple of seconds the eye movement decreases and the test is repeated to the left. The nystagmus is interpreted on direction, gain, start velocity, time constant and gesamtamplitude (GA; see table 2). The direction preponderance is also calculated and indicates which vestibular system responds stronger (it is normal if the ratio is below 25%).

Table 2. Norm values of adults and children of the VST

Norm values	Nystagmus direction	Gain	Start velocity v (^{0}/s)	Time constant τ (s)	Gesamtamplitude GA (^{0})
Adults	Left or right	33-72	30-65	11-26	485-1135
Children	Left or right	55-144	50-130	8-20	1000-1900

Bithermal caloric testing

This test measures the responses of the vestibular system on temperature change due to irrigation of the ear. It is done two times in each ear with two different temperatures (30 and 44^{0}C). After irrigating the water for 30 seconds, the patient lays in the dark with open eyes. The nystagmus is mainly assessed on the maximum slow phase velocity (MSPV). After a little time the door of the room is opened so that the patient can fixate. The nystagmus can be suppressed now (VOR suppression test). After closing the door again, the nystagmus can increase again until it fades out. The order of irrigation is right-warm, left-warm, left-cold and right-cold. This is retained for the reason that the nystagmus direction switches when the temperature is changed from warm to cold. These results can indicate whether the vestibular system shows areflexia, hyporeflexia, normal flexia or hyperreflexia (see table 3).

Table 3. Norm values of adults and children of the caloric testing

Parameter	Function	Warm (^{0}/s)	Cold (^{0}/s)
Maximum slow phase velocity (MSPV)	Normal	10-52	7-31
	Hyporeflexia	6-9	6
	Hyperreflexia	>52	>31
	Areflexia	0-5	0-5
Fixation suppression	Normal	Yes	Yes
	Deviant	No	No

Adjustments for pediatric applications

Attractive things can be used to get children's attention to enhance their participation during vestibular assessments. This could be lights, toys or other accessories for instance. Inspiration for these adjustments came from other vestibular labs. The student created applications from experiences so that they could be tested in the vestibular protocol. In addition to these applications, a literature search was done to assess whether new questionnaires were available for implementation. The questionnaires were searched for both adult and pediatric patients. The search was done in Pubmed with a combination of the following terms: “vestibular”, “equilibrium”, “unsteadiness”, “assessment”, “questionnaire”, “children”, “pediatric”, “quality of life”, “subjective”.

2.2 Ethical concerns

The study protocols were in accordance with the ethical standard of the Human Resources Committee (Commissie Mensgebonden Onderzoek (CMO) in Dutch) and with the Declaration of Helsinki for research involving human subjects (2013). Because the study consisted of retrospective data analysis, written informed consent could not be retrieved from the subjects. This approach was in accordance with the approval of the ethics committee. The patient information was anonymized in the database.

3. Results

The analyses are described separately for each experiment: the demographics, pre analyses and the final analyses to answer the research questions.

3.1 Experiment A: correlations in test results of adult patients with UVW

The results of agreement and correlations within and between vestibular tests such as the vHIT, VST, DHI and calorics, are shown below.

3.1.1 Demographics

The sample of experiment A consisted of 638 patients (M_{age}=57y, *SD*=15.3y, range=7.9-88.2y), consisting of 186 CI-patients and 452 VS-patients (see table 4). An interesting group in this sample, were the patients with deviant results on the calorics and the vHIT in the affected ear (defined as the impaired group: N=182, M_{age}=58.7y, *SD*=13.8y, range=21.5-88.2y). Within this sample were 27 CI-patients and 155 VS-patients. No significant differences were found for gender and affected side between the impaired and unimpaired group (respectively (χ^2(1, 456=638)=.010, *p*=.930) for gender and (χ^2(1, 456=638)=3.454, *p*=.066) for affected side). A significant difference was found between the groups when the CI- and VS-patients were compared (χ^2(1, 456=638)=25.276, *p*=.000).

Table 4. Demographics of experiment A

Demographics		
N		638
Etiology (CI:VS)		186:452
Age (*M*±*SD*)		57.0 ± 15.3
Sex (M:F)		331:307
Side (AD:AS)		338:300
Results by group		
Vestibular function	Unimpaired	Impaired
N	456	182
Etiology (CI:VS)	159:297	27:155
Age (*M*±*SD*)	56.4 ± 15.8	58.7 ± 13.8
Sex (M:F)	236:220	95:87
Side (AD:AS)	231:225	107:75

3.1.2 Group differences and correlations within vestibular tests

The group differences and correlations are described per vestibular test in this section. A summary of the means and standard deviations are given per group (see table 5).

Table 5. Means and standard deviations per group *(M±SD).*

Vestibular test	Impaired	Unimpaired	CI	VS
VST				
Velocity	51.0 ± 20.0	59.4 ± 20.3	56.8 ± 22.8	57.0 ± 19.7
Time constant	9.5 ± 4.3	12.9 ± 4.4	11.5 ± 4.9	12.1 ± 4.5
Gesamtamplitude	491 ± 277	760 ± 346	658 ± 348	692 ± 349
Caloric MSPVs				
Warm	1.52 ± 2.15	15.12 ± 11.49	13.9 ± 11.6	9.8 ± 11.3
Cold	1.61 ± 1.81	13.33 ± 7.11	11.4 ± 8.2	9.0 ± 7.9

vHIT gains				
Anterior SCC	.71 ± .26	.97 ± .13	.94 ± .20	.88 ± .21
Lateral SCC	.60 ± .28	.96 ± .10	.94 ± .18	.83 ± .25
Posterior SCC	.58 ± .28	.84 ± .18	.82 ± .25	.74 ± .24
DHI scores				
Physical	7.7 ± 7.2	5.5 ± 6.5	4.2 ± 5.7	6.9 ± 7.1
Functional	7.1 ± 8.4	5.6 ± 7.5	4.2 ± 6.3	6.8 ± 8.2
Emotional	5.0 ± 6.0	3.7 ± 5.7	2.8 ± 4.9	4.6 ± 6.1
Total	20.0 ± 20.1	14.8 ± 18.4	11.1 ± 15.7	18.2 ± 19.8

Velocity Step Test

The sample consisted of 625 patients (CI:VS=182:443; impaired:unimpaired=181:444), because 13 patients were not measured by the VST. The three variables of the VST (velocity, time constant and gesamtamplitude (GA)) were analysed to assess whether significant group differences existed between the impaired and unimpaired group and between the VS- and CI-group. For the GA, a continuous variable of the absolute values and a categorical variable was created to see whether diagnostic labels had a different effect than the absolute values. The categorical variable was defined in three labels: hypoactivity, normal activity and hyperactivity (see table 2 for values).

In the two-way ANOVA a significant effect was found for impairment for all the variables of VST (velocity, $F(1, 621)=12.087$, $p=.001$, $\eta^2=.019$; time constant, $F(1, 621)=82.892$, $p=.000$, $\eta^2=.102$; $GA_{continuous}$, $F(1, 621)=70.368$, $p=.000$, $\eta^2=.102$; $GA_{categorical}$, $F(1, 621)=67.210$, $p=.000$, $\eta^2=.098$). The impaired group showed results below the norm values for time constant (see figure 3b) and GA (see figure 3c), whereas the unimpaired group revealed normal results. For velocity both groups showed values within the normal range (see figure 3a).

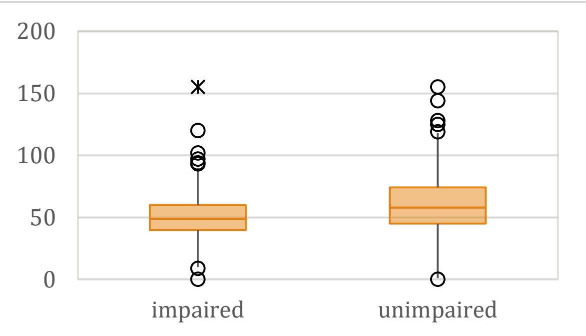


Figure 3a. Boxplot VST velocity – group differences between the impaired and unimpaired group. The means of the groups differed significantly, but were both within the normal range.

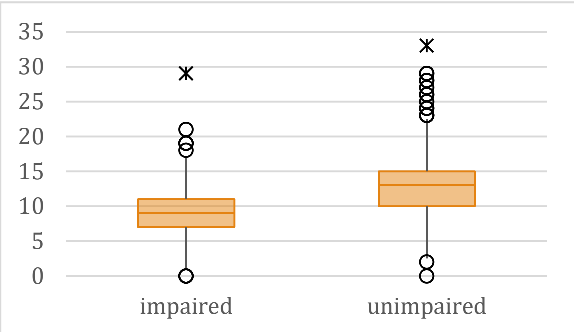


Figure 3b. Boxplot VST time constant – group differences between the impaired and unimpaired group. The mean of the impaired group was below the normal range, whereas the unimpaired had a mean within the normal range. This resulted in a significant difference between the groups.

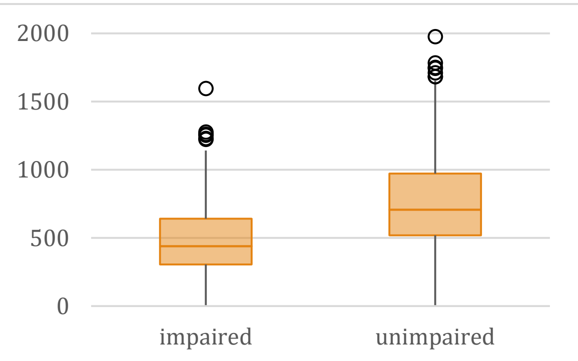


Figure 3c. Boxplot VST GA – group differences between the impaired and unimpaired group. The mean of the impaired group was near the lower limit, whereas the unimpaired group had a mean within the normal range. This resulted in a significant difference between the groups.

Between the CI- and VS-group, significant differences were found for time constant ($F(1, 621)=18.513$, $p=.000$, $\eta^2=.026$), $GA_{continuous}$ ($F(1, 621)=10.060$, $p=.002$, $\eta^2=.016$) and $GA_{categorical}$ ($F(1, 621)=7.122$, $p=.008$, $\eta^2=.098$). An interaction effect of impairment and patient group was only significant for time constant ($F(1, 621)=8.032$, $p=.005$, $\eta^2=.010$). Both groups had results within the normal range for velocity (see figure 4a). For time constant the results were on the lower limit of the normal range (see figure 4b). The GA results were within the normal range (see figure 4c).

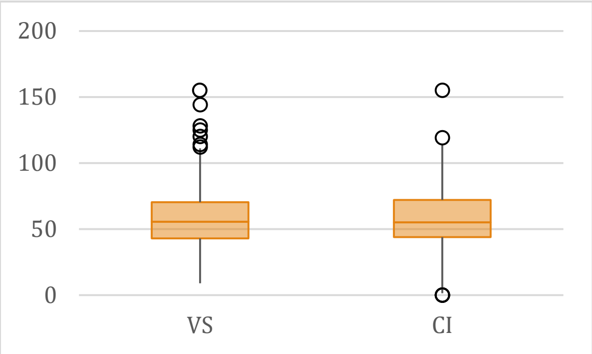


Figure 4a. Boxplot VST velocity – group differences between the VS- and CI-group. No significant group difference was found between the two means of the patient groups. The means of both groups were near the upper limit of the normal range.

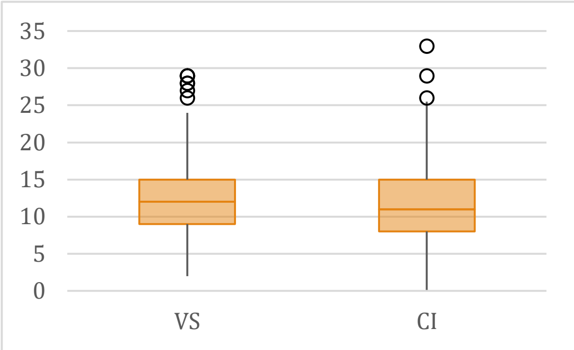


Figure 4b. Boxplot VST time constant – group differences between the VS- and CI-group. A significant difference was found between the patient groups. Both means were near the lower limit of the normal range.

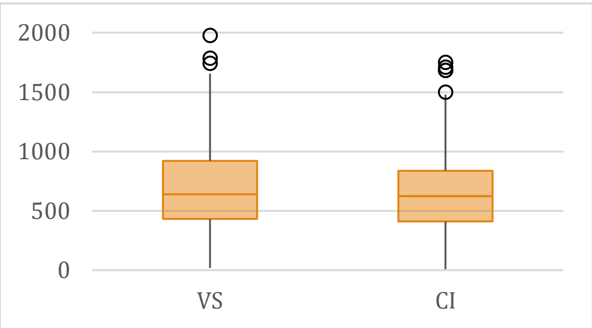


Figure 4c. Boxplot VST GA – group differences between the VS- and CI-group. The means of both groups were within the normal range. A significant difference was found between the means of the patient groups.

In the Pearson correlation tests significant correlations were found for GA with velocity ($r=.650$, $p=.000$) or time constant ($r=.727$, $p=.000$), but these are less relevant due to the fact that GA=velocity*time constant. The most interesting correlation exists between velocity and time constant and it was significant (see figure 5, $r=.103$, $p=.009$).

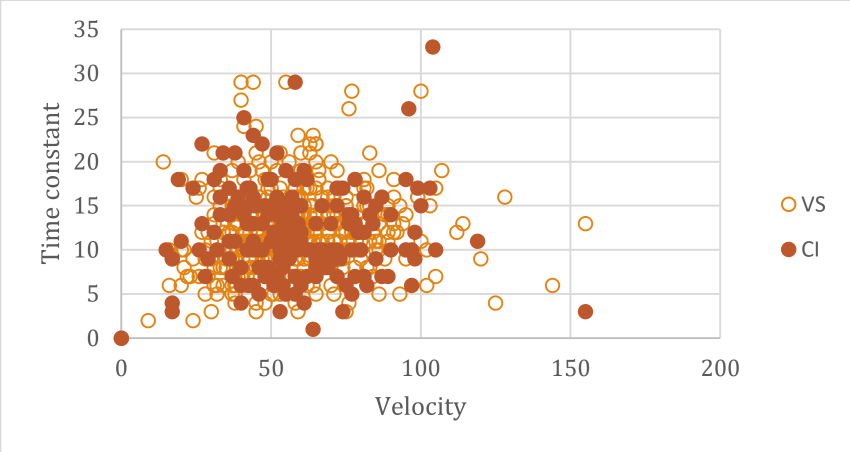


Figure 5. Scatterplot VST velocity and time constant – A significant correlation was found between time constant and velocity.

Calorics

The sample consisted of 562 patients(CI:VS=146:416; impaired:unimpaired=178:384), due to incomplete data of 76 patients. The caloric results of this sample were compared between the impaired and the unimpaired group and between the CI- and VS-group. For both warm and cold calorics, a continuous and a categorical variable of the maximum slow phase velocity (MSPV) were created to see whether the diagnostic labels showed different effects than the absolute values. The categorical variables were defined in areflexia, hyporeflexia, normal reflexia and hyperreflexia (see table 3 for values).

In the two-way ANOVA, a significant effect of impairment was found on the MSPV of all parameters of the calorics (warm$_{continuous}$, $F(1, 558)=140.240$, $p=.000$, $\eta^2=.201$; warm$_{categorical}$ $F(1, 558)=503.634$, $p=.000$, $\eta^2=.474$; cold$_{continuous}$, $F(1, 558)=273.880$, $p=.000$, $\eta^2=.329$; cold$_{categorical}$, $F(1, 558)=1174.811$, $p=.000$, $\eta^2=.678$). The unimpaired group had means within the normal range, whereas the impaired group had means below the normal range (see figure 6a-b).

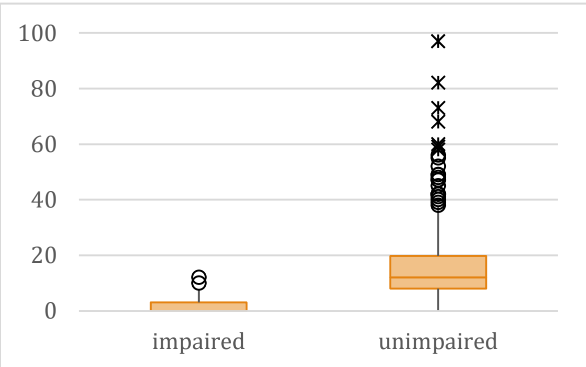


Figure 6a. Boxplot MSPV warm calorics – group differences between the impaired and unimpaired group. A significant difference was found between the two groups. The impaired group had a mean below the normal range, whereas the unimpaired group had a mean within the normal range.

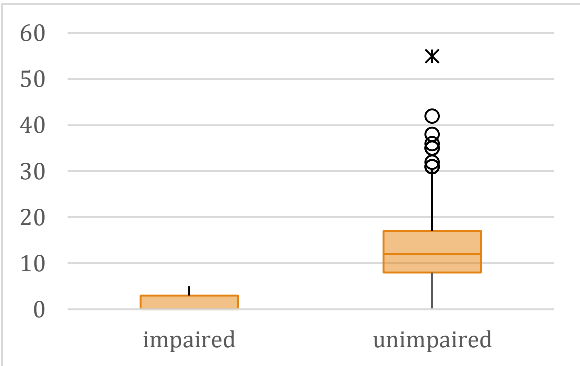


Figure 6b. Boxplot MSPV cold calorics – group differences between the impaired and unimpaired group. The mean of the impaired group was below the normal range, while the mean of the unimpaired group was within the normal range. The means of both groups differed significantly.

For the difference in patient group, only a significant difference was found for the MSPV of the warm$_{categorical}$, $F(1, 558)=4.737$, $p=.030$, $\eta^2=.008$). The CI-patients had means within the normal range for the warm calorics (see figure 7a). The VS-patients had means below the normal range for the warm calorics. For the cold calorics both patient groups had means within the normal range (see figure 7b). No interaction effects of impairment and patient group were significant (*ps*>.05).

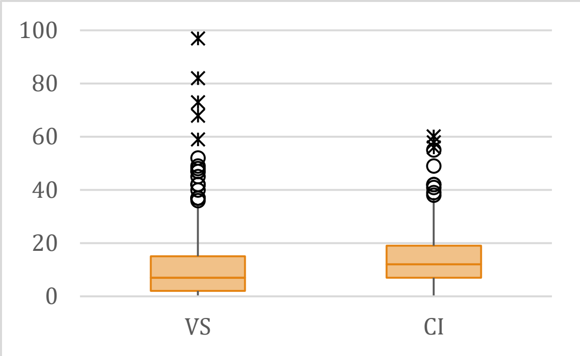


Figure 7a. Boxplot MSPV warm calorics – group differences between the VS- and CI-group. The VS-group had a mean below the normal range, while the CI-group had a mean within the normal range. This resulted in a significant difference between the patient groups for the warm calorics$_{categorical}$.

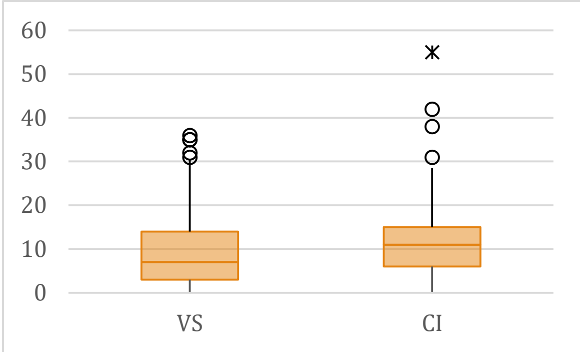


Figure 7b. Boxplot MSPV cold calorics – group differences between the VS- and CI-group. Both groups had a mean within the normal range. The means did not differ significantly.

In the Pearson correlation test, a significant correlation was found between the MSPVs of the warm and cold calorics for both continuous and categorical variables (see figure 8, continuous, *r*=.737, *p*=.000; categorical, *r*=.767, *p*=.000).

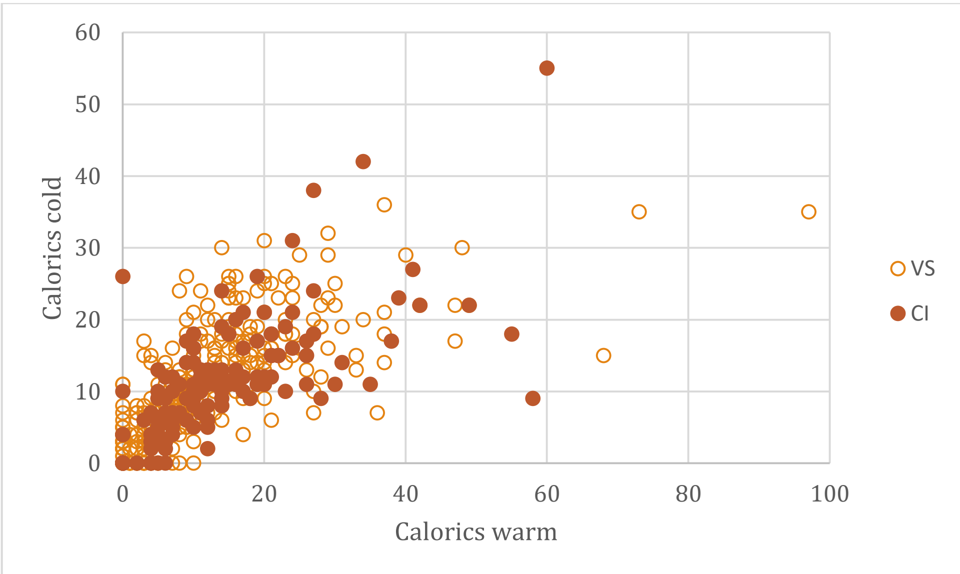


Figure 8. Scatterplot MSPV warm and cold calorics – A significant correlation was found between the MSPVs of the warm and cold calorics.

Video Head Impulse Test

The vHIT results were compared between the impaired and unimpaired group and between the CI- and VS-group (N=483; CI:VS=140:343; impaired:unimpaired=140:343). Due to the fact that the vHIT was introduced in the clinical setting during the included period, 155 patients had no results on this test. For each SCC a continuous and a dichotomous variable was created to differ between impaired and unimpaired results. The dichotomous variable was defined deviant when the anterior gain was <.74, the lateral gain <.81 and the posterior gain <.78. Higher results were considered normal.

In the two-way ANOVA, a significant effect was found for impairment on all variables (anterior$_{continuous}$, F(1, 479)=119.924, *p*=.000, η^2=.200; anterior$_{dichotomous}$, F(1, 479)=104.813, *p*=.000, η^2=.180; lateral$_{continuous}$, F(1, 479)=215.866, *p*=.000, η^2=.311; lateral$_{dichotomous}$, F(1, 479)=195.373, *p*=.000, η^2=..290 posterior$_{continuous}$, F(1, 479)=101.008, *p*=.000, η^2=.174; posterior$_{dichotomous}$, F(1, 479)=69.400, *p*=.000, η^2=.127). The unimpaired group had means within the normal range of vHIT gains (see figures 9a-c). The impaired group had a mean near the lower limit for the gain of the anterior SCC and below the normal range for the gains of the lateral SCC and the posterior SCC.

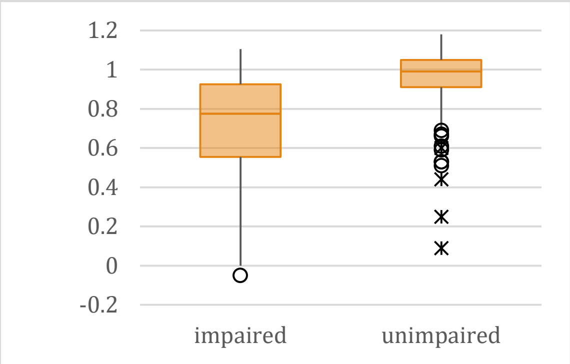


Figure 9a. Boxplot vHIT gain anterior SCC - group differences between the impaired and the unimpaired group. The impaired group had a mean near the lower limit of the normal range, while the unimpaired group had a mean in the normal range. This difference in means between the groups was significant.

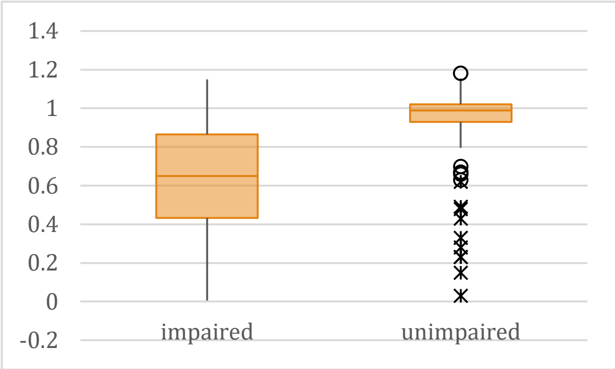


Figure 9b. Boxplot vHIT gain lateral SCC – group differences between the impaired and the unimpaired group. The impaired group had a mean below the normal range, while the unimpaired group had a mean within the normal range. This resulted in a significant difference between the groups.

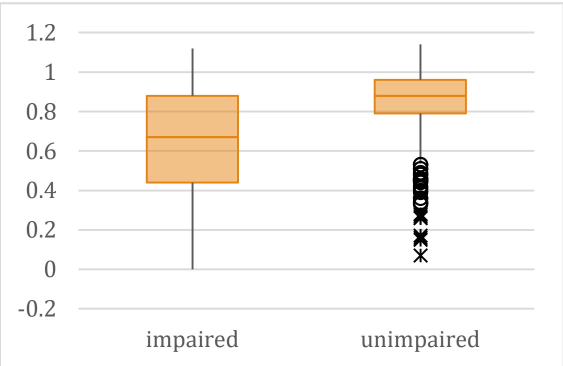
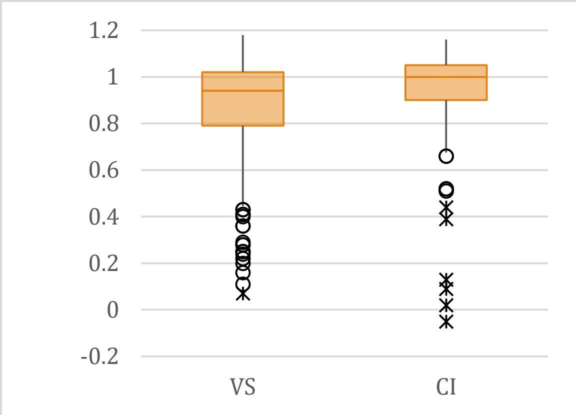


Figure 9c. Boxplot vHIT gain posterior SCC – group differences between the impaired and the unimpaired group. The impaired group had a mean below the normal range, while the mean of the unimpaired group was within the normal range. This resulted in a significant difference.

The effect of difference in patient group was only significant for the lateral SCC, both continuous ($F(1, 479)=8.665$, $p=.003$, $\eta^2=.018$) and dichotomous results ($F(1, 479)=10.502$, $p=.001$, $\eta^2=.021$). The CI-group had a mean within the normal range (see figure 10b) for the lateral SCC, while the VS-group had a mean near the lower limit. For the gain of the anterior SCC, both VS- and CI-group had means within the normal range (see figure 10a). The gain of the posterior SCC was within the normal range for the CI-group (see figure 10c), but not for the VS-group. A significant interaction effect of impairment and patient group was found for the lateral $SCC_{dichotomous}$ ($F(1, 479)=5.899$, $p=.016$, $\eta^2=.012$).



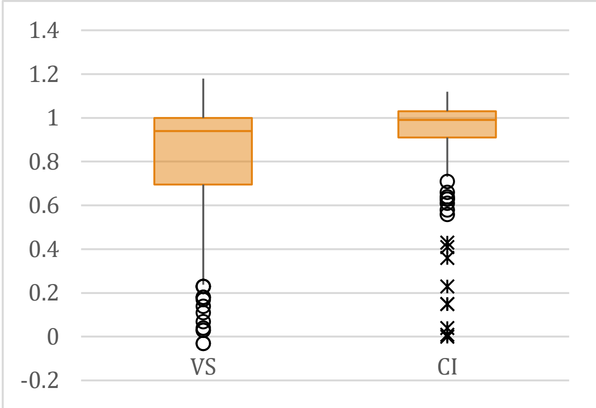


Figure 10a. Boxplot vHIT gain anterior SCC – group differences between the VS- and CI-group. The medians of the gains of both groups are higher than the means, but the difference in means is not significant.

Figure 10b. Boxplot vHIT lateral SCC– group differences between the VS- and CI-group. The mean of the gain of the CI-group was within the normal range, while the mean of the VS-group was near the lower limit. This resulted in a significant difference between the groups.

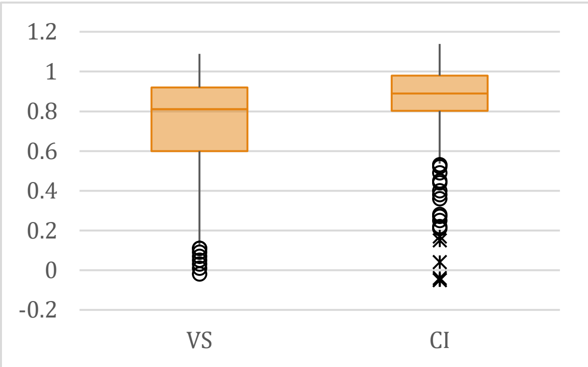


Figure 10c. Boxplot vHIT posterior SCC – group differences between the VS- and CI-group. The median of the gain of the posterior gain was within the normal range for both patient groups, while the mean of the VS-group was below the lower limit.

In the Pearson correlation test significant correlations were found between all the SCCs (see table 6). In the scatterplots not all correlations seem to be the same between the CI- and VS-patients (see figures 11a-c). Only the correlation between the gains of the anterior and posterior canal the lines seem to be the same. The separate patient group correlations were tested in Pearson correlation tests and in both groups the significant correlations between the SCCs remained (see table 6). The correlations of the anterior SCC with one of the other SCCs differed not significantly between the two patient groups (see table 6, z=.753, two-tailed, *p*>.05 for anterior*lateral; z=.658, two-tailed, *p*>.05 for anterior*posterior). However, for the correlation between the lateral and the posterior SCCs a significant difference between the VS- and CI-patients was found (z=2.952, two-tailed, *p*=.003).

Table 6. Correlations between semicircular duct gains of the vHIT

Correlation	*r*	*p*
CI+VS (N=483)		
Anterior*Lateral	.683	**
Anterior*Posterior	.596	**
Lateral*Posterior	.580	**
CI (N=140)		
Anterior*Lateral	.649	**
Anterior*Posterior	.615	**
Lateral*Posterior	.709	**
VS (N=343)		
Anterior*Lateral	.690	**
Anterior*Posterior	.577	**
Lateral*Posterior	.535	**

**=p<.01, *=p<.05

**

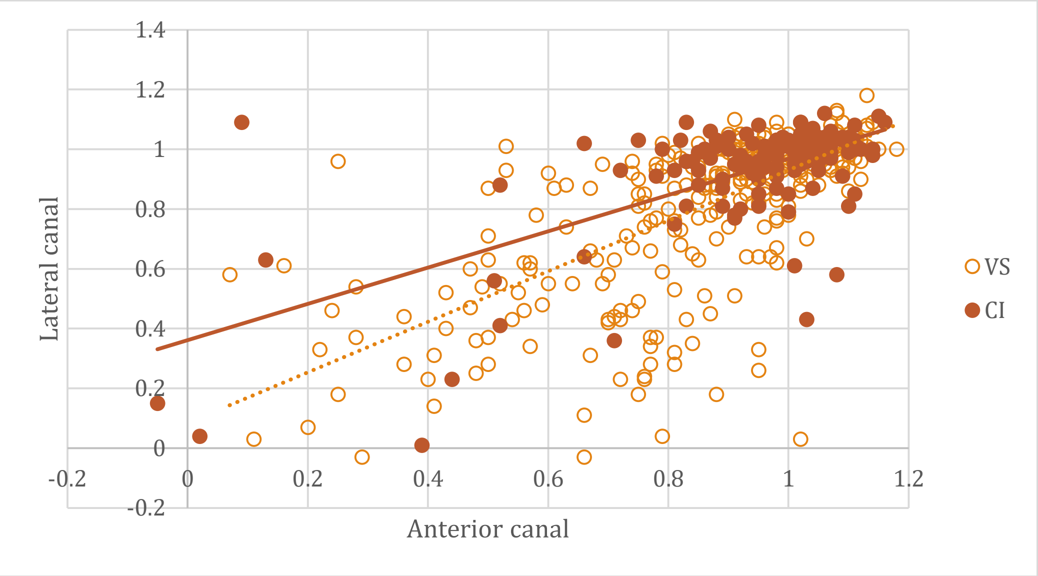


Figure 11a. Scatterplot vHIT gains of the anterior and lateral SCCs – A significant correlation was found between the gains of the anterior and lateral SCCs. These remained significant when the correlations were tested in the separate patient groups. The correlations between the groups did not differ significantly.

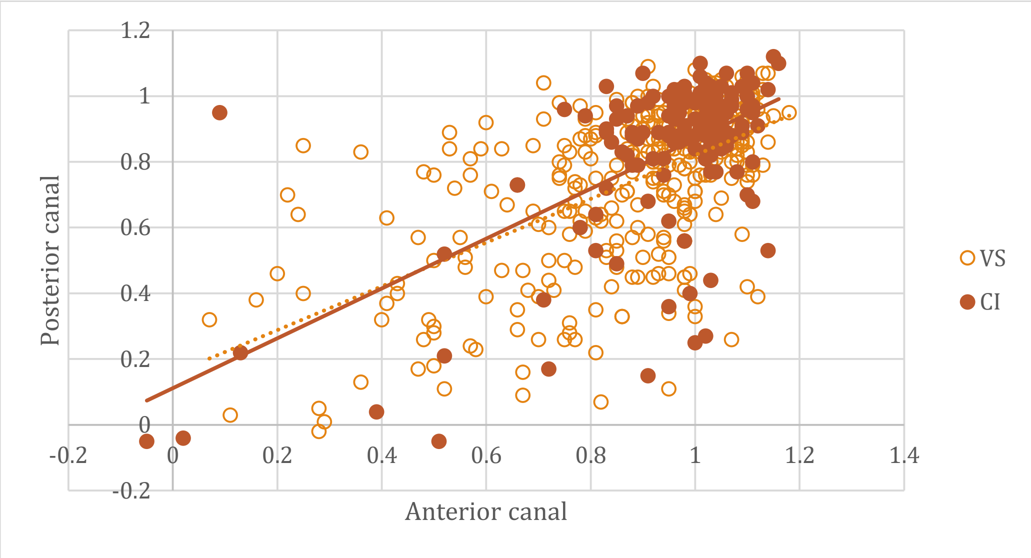


Figure 11b. Scatterplot vHIT gains of the anterior and posterior SCCs – The correlation between the gains of the anterior and posterior SCCs was significant, in the whole sample and in the separate patient groups. The correlations were not significantly different between the groups.

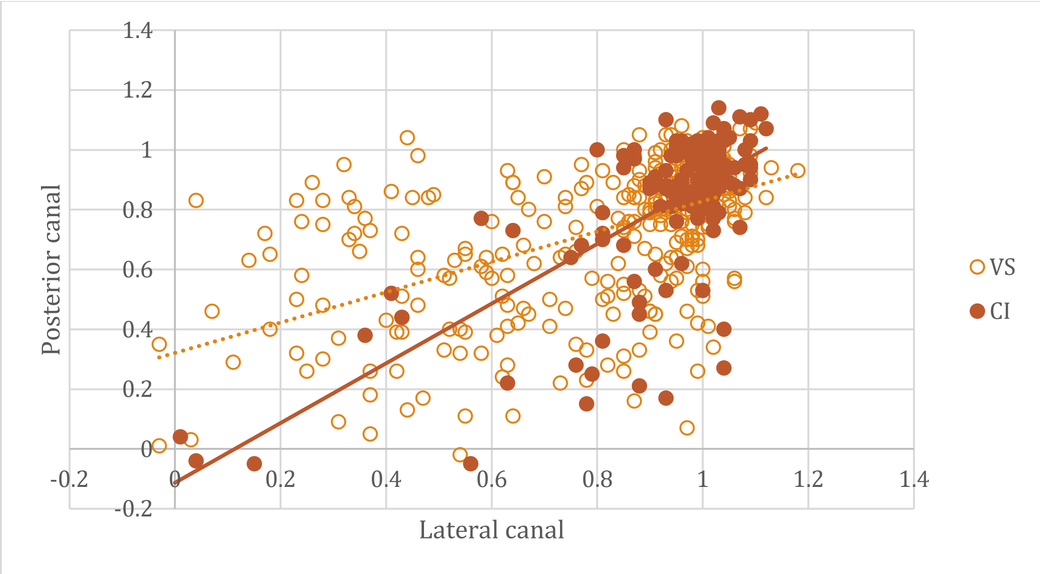


Figure 11c. Scatterplot vHIT gains of the lateral and posterior SCCs – The gains of the lateral SCC and the posterior SCC correlated significantly, in the whole sample and in the separate patient groups. The correlations between the patient groups differed significantly.

Dizziness Handicap Inventory

The sample of patients consisted of 597 individuals, due to the fact that 42 patients did not complete the questionnaire. A categorical variable was created with three labels: mild handicap (total score 0-30), moderate handicap (total score 31-60) and severe handicap (total score 61-100). Most patients had a mild handicap (74.6%), while most others had a moderate handicap (22 CI- and 80 VS-patients). A severe handicap was seen in 3.1% of the patients, based on these labels (1 CI- and 18 VS-patients). All scores of the DHI were assessed on group differences between the impaired and the unimpaired group and between the CI- and the VS-group. A two-way ANOVA showed significant differences for impairment on all DHI-scores (physical, $F(1, 593)=13.057$, $p=.000$, $\eta^2=.022$; functional, $F(1, 593)=7.212$, $p=.007$, $\eta^2=.012$; emotional, $F(1, 593)=8.479$, $p=.004$, $\eta^2=.014$; total, $F(1, 593)=10.924$, $p=.001$, $\eta^2=.018$). The means of all sub scores were low in the ranges for both the impaired group (see figures 12a-c) and the unimpaired group. The means of the total score were also low and were in the category of a mild handicap (see figure 12d).

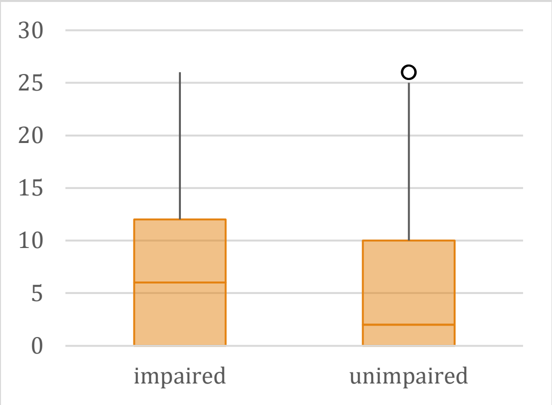


Figure 12a. Boxplot DHI physical score - group differences between the impaired and unimpaired group. The mean of the unimpaired group is higher than the median, but the means still differ significantly.

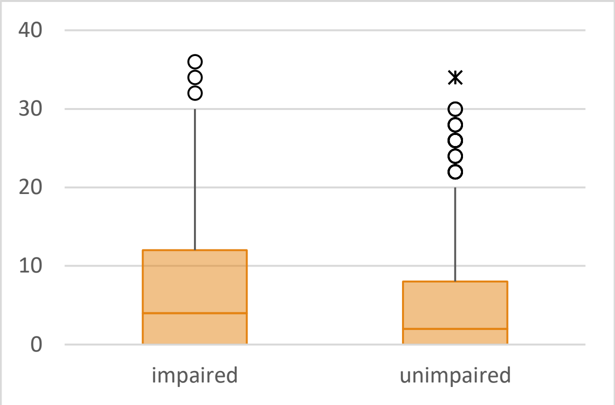


Figure 12b. Boxplot DHI functional score – group differences between the impaired and unimpaired group. A significant difference was found between the means of the groups. The median of the unimpaired group is lower than its mean.

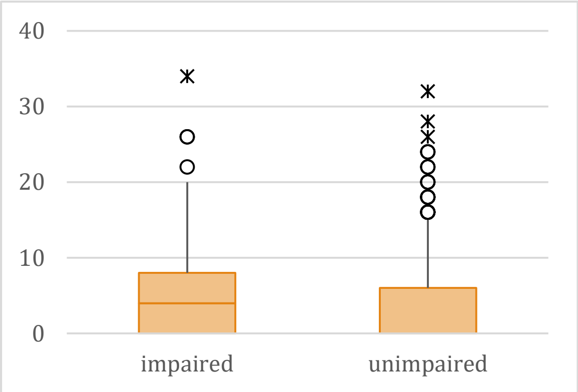


Figure 12c. Boxplot DHI emotional score – group differences between the impaired and unimpaired group. The means between the groups differed significantly.

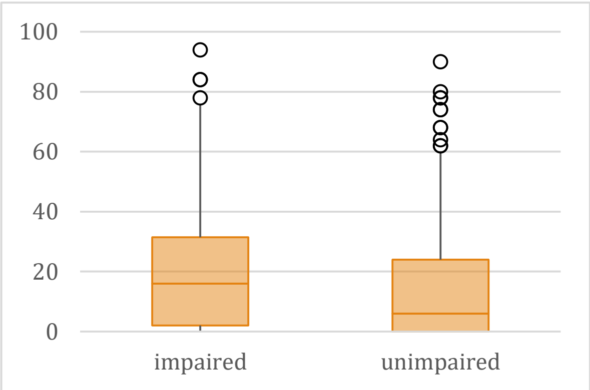


Figure 12d. Boxplot DHI total score – group differences between the impaired and unimpaired group. The means of both groups were in the category of mild handicap, but differed significantly.

The difference between the CI- and VS-group did not have a significant effect on the DHI-scores (*ps*>.05). But a significant interaction-effect of impairment and patient group existed on all DHI-scores (physical, $F(1, 593)=4.984$, $p=.026$, $\eta^2=.008$; functional, $F(1, 593)=5.842$, $p=.016$, $\eta^2=.010$; emotional, $F(1, 593)=5.569$, $p=.019$, $\eta^2=.009$; total, $F(1, 593)=6.356$, $p=.012$, $\eta^2=.011$). The means of the sub scores did not differ much between the different scores, although the distribution was relatively spread (see figures 13a-c). The means of the total score were for both patient groups in the category mild handicap (see figure 13d).

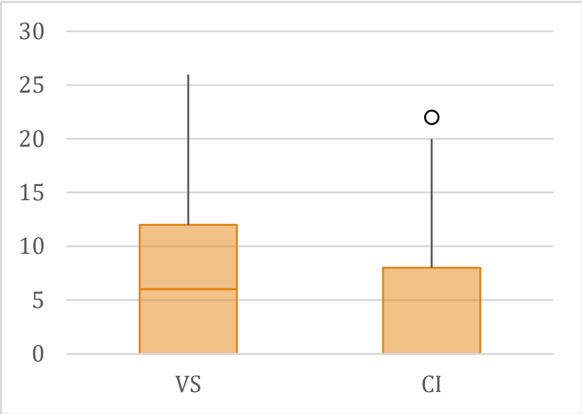


Figure 13a. Boxplot DHI physical score – group differences between the VS- and CI-group. The means of both patient groups were low and this did not result in a significant difference between the groups.

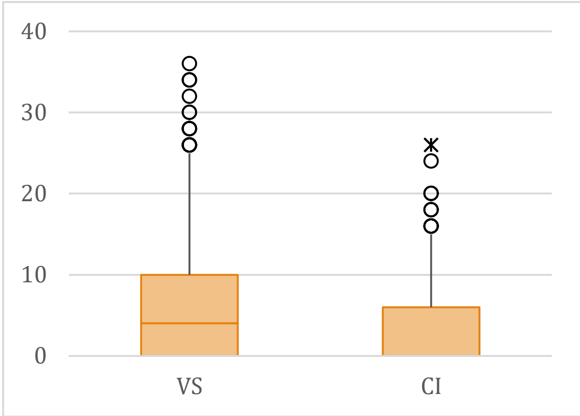


Figure 13b. Boxplot DHI functional score – group differences between the VS- and the CI-group. The means of the patient groups did not differ significantly.

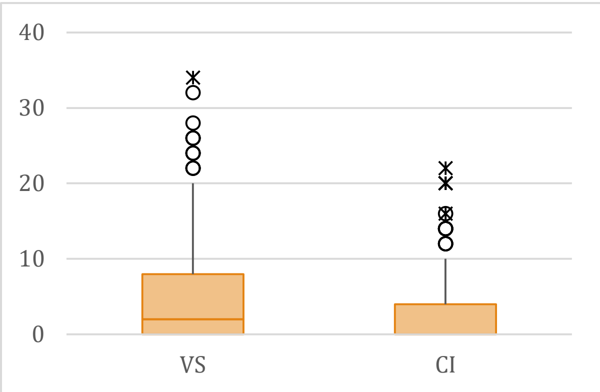


Figure 13c. Boxplot DHI emotional score – group differences between the VS- and CI-group. The means of the patient groups did not differ significantly.

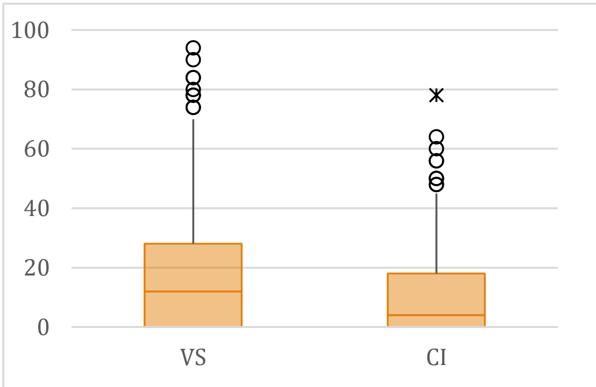


Figure 13d. Boxplot DHI total score – group differences between the VS- and CI-group. This difference in the means of the patient groups was not significant.

The Pearson's correlation tests revealed that all DHI scores correlated with the total score (physical*total, r=.915, p=.000; functional*total, r=.958, p=.000; emotional*total, r=.906, p=.000). These correlations are predictable, due to the fact that the total score is the sum of the sub scores. But also the sub scores correlated mutually (see figures 14a-c; physical*functional, r=.817, p=.000; physical*emotional, r=.719, p=.000; functional*emotional, r=.829, p=.000).

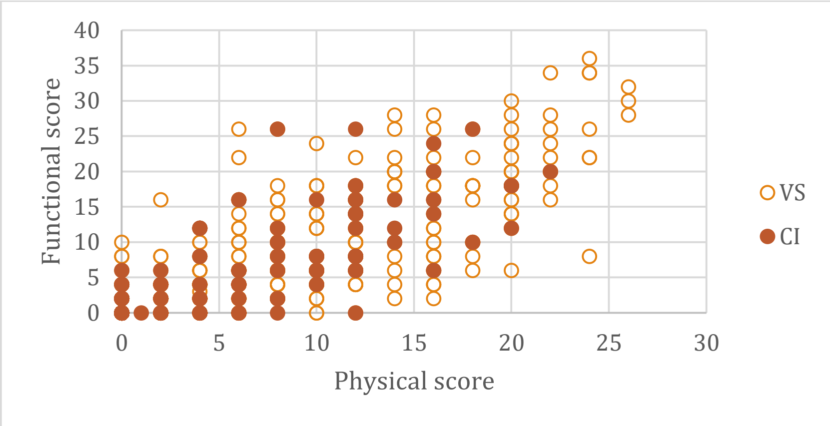


Figure 14a. Scatterplot DHI physical and functional scores – The correlation between the physical and functional score was significant.

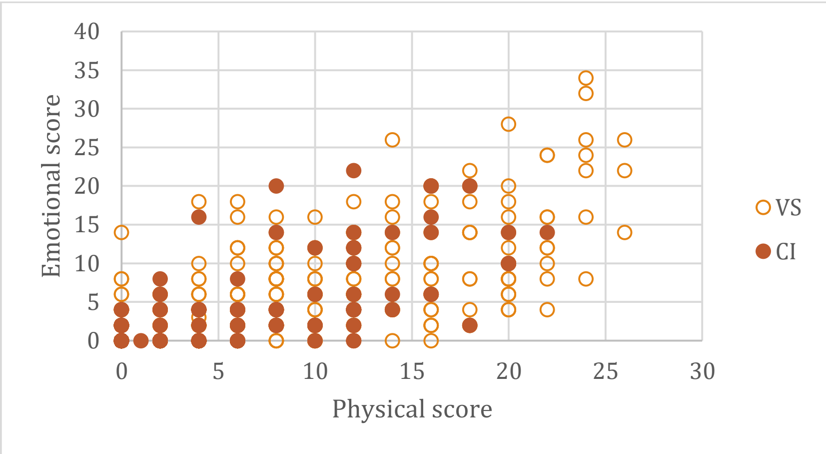


Figure 14b. Scatterplot DHI physical and emotional scores – The correlation between the physical and emotional score was significant.

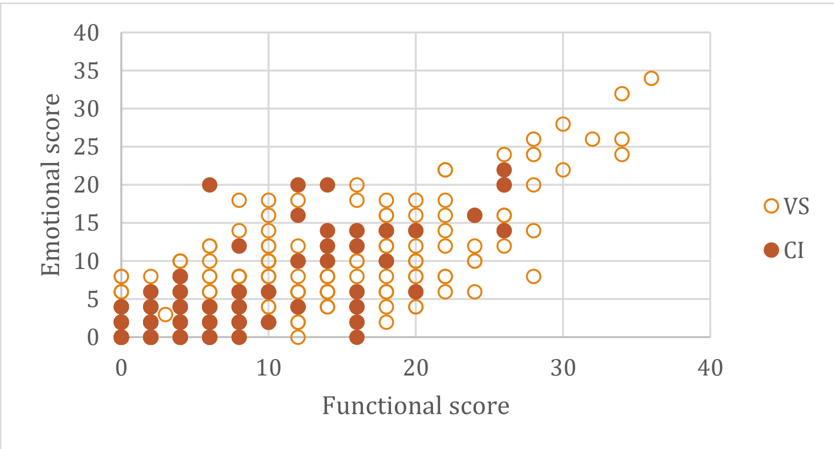


Figure 14c. Scatterplot DHI functional and emotional scores – The correlation between the functional and emotional score was significant.

Conclusion group differences within vestibular tests

All vestibular tests were analysed on group differences between the impaired and unimpaired group and between the VS- and CI-group. The differences between the impaired and the unimpaired group were significant for all sub tests (see table 7). The difference in patient group (VS or CI) only effected the time constant and GA of the VST, the MSPV of the warm calorics$_{categorical}$ and the gain of the lateral duct of the vHIT. These differences had weak effects, which meant that they had very little effect on the vestibular test results. This resulted in pooling the patient groups together for further analyses.

Table 7. Significant group differences in vestibular tests

Vestibular test	Impaired vs. unimpaired		VS vs. CI	
	p	η^2	*p*	η^2
VST				
Velocity	**	.019	n.s.	
Time constant	**	.102	**	.026
Gesamtamplitude	**	.102	**	.016
Calorics (MSPV)				
Warm	**	.201	*	.008
Cold	**	.329	n.s.	
vHIT (gain)				
Anterior canal	**	.200	n.s.	
Lateral canal	**	.311	**	.018
Posterior canal	**	.174	n.s.	
DHI				
Physical score	**	.022	n.s.	
Functional score	**	.007	n.s.	
Emotional score	**	.014	n.s.	
Total score	**	.018	n.s.	

**=p<.01, *=p<.05

3.1.3 Correlations between vestibular (sub) tests

In the prior analyses became clear that that the CI and VS-patients could be pooled together in these analyses. Also the correlations within vestibular tests were assessed, while in this section the correlations between sub tests were examined to answer the research questions. This resulted the following table (see table 8).

Table 8. Correlations between vestibular sub tests

		VST			Calorics		vHIT		
	Sub test	Velocity	Time constant	GA	Warm	Cold	Anterior	Lateral	Posterior
VST	Velocity								
	Time constant								
	GA								
Calorics (MSPV)	Warm	.25**	.35**	.38**					
	Cold	.25**	.43**	.44**					
vHIT (gain)	Anterior	.18**	.26**	.29**	.32**	.41**			
	Lateral	.29**	.36**	.41**	.44**	.52**			
	Posterior	.201**	.28**	.30**	.32**	.42**			
DHI	Physical	n.s.	-.11**	n.s.	-.11*	-.17**	-.13**	-.18**	-.14**
	Functional	n.s.	-.10*	n.s.	n.s.	-.14**	-.14**	-.16**	-.16**
	Emotional	n.s.	-.08*	n.s.	-.09*	-.16**	-.11*	-.14**	-.14**
	Total	n.s.	-.11*	n.s.	-.10*	-.17**	-.14**	-.17**	-.16**

**=p<.01, *=p<.05

Table 8 showed that the parameters of the VST, calorics and vHIT all correlate positively (p<.01). The scores of the DHI correlated negatively with the vHIT gains, the time constant of the VST and the MSPV of the calorics. The only exception was the functional score of the DHI: it did not correlate with the MSPV of the warm calorics (p>.05). The VST parameters and the DHI scores did not correlate significantly on velocity and gesamtamplitude (GA) (ps>.05). All these significant correlations had weak effectsizes (η^2<.6).

3.1.4 Prediction model of impaired vestibular function

The correlations between the tests indicate a weak cohesion of the vestibular tests, but do not answer the research questions of experiment A fully. To answer the first research question, which objective vestibular function test results agree with the DHI score in adult patients with VS and CI, a multiple regression and a multinomial logistic regression were conducted. The former significant correlations between the tests suggest that the vHIT gains and caloric results could potentially predict DHI scores.

Model 1: prediction model of DHI total score

In the multiple regression, all parameters of the VST, calorics and vHIT were put in as predictors of the DHI total score. Using both the forward and backward method, it was found that the gain of the posterior canal and the cold caloric MSPV explained a significant amount of the variance in the total DHI score (F(2, 401)=10.295, p=.000, R^2=.049, R^2 *adjusted*=.044). The analysis showed that the MSPV of the cold calorics significantly predicted the total score of the DHI (see table 9 step 1, *Beta*=-.149, t(396)=-2.778, p<.01), as did the gain of the posterior canal (*Beta*=-.111, t(396)=-2.067, p<.05). Using the categorical variables instead of the absolute values did not change the model.

In contradiction to the former analyses, the model changed when the difference in patient group was added to the analysis (see table 9 step 2). Using the forward method, the predictor gain of the posterior canal was replaced in the model by the difference in patient group (F(2, 401)=10.837, p=.000, R^2=.051, R^2 *adjusted*=.047). The prediction effect of the MSPV of the cold calorics on the DHI total score changed a little (*Beta*=-.182, t(395)=-3.705, p=.000). The difference in patient group predicted significantly the total DHI score (*Beta*=.113, t(395)=2.305, p=.022). When the age of the participants at time of testing was added as predictor, it was included in the model with the MSPV of the cold calorics and difference in patient group (see table 9 step 3, F(3, 400)=9.219, p=.000, R^2=.065, R^2*adjusted*=.058). In this model, the MSPV of the cold calorics still explained significantly the total score of the DHI (*Beta*=-.170, t(394)=-3.475, p=.001), as did patient group (*Beta*=.100, t(395)=2.044, p=.042). The age at time of testing also explained the DHI total score significantly (*Beta*=.117, t(394)=2.393, p=.017). In the last step, gender was added as predictor and this resulted in a significant addition to the model (see table 9 step 4, F(4, 399)=9.533, p=.000, R^2=.087, R^2*adjusted*=.078). In this model, significant predictors of the total DHI score were the MSPV of the cold calorics (*Beta*=-.172, t(393)=-3.541, p=.000), gender (*Beta*=.151, t(393)=3.140, p=.002), age at time of testing (*Beta*=.134, t(393)=2.751, p=.006) and difference in patient group (*Beta*=.107, t(393)=2.199, p=.028).

The multiple regression was run again to assess if the sub tests of the VST, the calorics and vHIT could predict one of the sub scores of the DHI. Using the forward method, the model only contained the cold calorics as predictor of the physical DHI score (F(2, 401)=13.965, p=.000, R^2=.034, R^2 *adjusted*=.031). The MSPV of the cold calorics predicted significantly the physical score of the DHI (*Beta*=-.183, t(396)=-3.737, p=.000). Using the forward method, the model contained cold calorics and the vHIT gain of the posterior canal to significantly predict the functional score (F(2, 401)=13.426, p=.000, R^2=.043, R^2 *adjusted*=.039). The gain of the posterior canal explained most of the variance (*Beta*=-.131, t(395)=-2.419, p=.016), while the MSPV of the cold calorics also significantly predicted the functional score of the DHI (*Beta*=-.116, t(396)=-2.144, p=.033). In the analysis of the emotional score of the DHI, only the cold calorics was included as significant predictor (F(2, 401)=16.010, p=.000, R^2=.038, R^2 *adjusted*=.036). The cold calorics explained a significant amount of variance of the emotional score of the DHI (*Beta*=-.196, t(396)=-4.001, p=.000).

Table 9. Stepwise results of the multiple regression

	b	SE	β	*p*
Step 1				
Constant	26.572	3.015		
MSPV Cold calorics	-.364	.131	-.149	.006
Gain posterior canal	-8.666	4.193	-.111	.039
Step 2				
Constant	12.097	4.184		
MSPV Cold calorics	-.442	.119	-.182	.000
Patient group	4.984	2.163	.113	.022
Step 3				
Constant	3.778	5.418		
MSPV Cold calorics	-.414	.119	-.170	.001
Age at time of testing	.158	.066	.117	.017
Patient group	4.421	2.163	.100	.042
Step 4				
Constant	-6.573	6.294		
MSPV Cold calorics	-.418	.118	-.172	.000
Gender	5.845	1.861	.151	.002
Age at time of testing	.181	.066	.134	.006
Patient group	4.708	2.141	.107	.028

Model 2: prediction model of DHI categories

A multinomial logistic regression was performed to assess whether the sub tests of the VST, calorics and vHIT could predict the categories of the DHI score (0-30 mild handicap, 31-60 moderate handicap, 61-100 severe handicap). Using the forward method, it was found that the time constant of the VST and the cold calorics significantly explained variance of the DHI labels, $\chi^2(4)=17084$, $p=.002$ (see table 10). The time constant of the VST predicted significantly the labels of the DHI score, $\chi^2(2)=6.560$, $p=.038$, as did the MSPV of the cold calorics, $\chi^2(2)=7.652$, $p=.022$. The time constant of the VST significantly predicted whether a patient was labelled in the category mild handicap or moderate handicap, $b=-.078$, Wald $\chi^2(1)=4.738$, $p=.030$. The odds ratio (.925) meant that if the time constant increased, the chance to be labelled in the moderate handicap instead of the mild handicap decreased. The MSPV of the cold calorics did not significantly predict the chance that a patient was labelled as mild handicap or moderate handicap, $b=-.029$, Wald $\chi^2(1)=2.025$, n.s., while it did for the chance that a patient was labelled correct in the severe handicap category or the mild handicap category, $b=-.108$, Wald $\chi^2(1)=4.803$, $p=.028$.The time constant of the VST did not significantly predict the chance that a patient was labelled in the category severe handicap instead of mild handicap, $b=.059$, Wald $\chi^2(1)=1.067$, n.s. The odds ratio (.898) meant that if the MSPV of the cold calorics increased, the chance on the label severe handicap versus the label mild handicap would decrease.

Table 10. Results of the multinomial logistic regression

	b (SE)		95% CI for Odds Ratio		
			Lower	Odds ratio	Upper
Mild handicap vs. Moderate handicap					
Intercept	-.379 (.383)				
Time constant	-.078 (.036)	*	.862	.925	.992
MSPV Cold calorics	-.029 (.020)		.934	.972	1.011
Mild handicap vs. Severe handicap					
Intercept	-3.029 (.738)	**			
Time constant	.059 (.057)		.949	1.061	1.186
MSPV Cold calorics	-.108 (.049)	*	.815	.898	.989

*=p<.05, **=p<.01

Model 3: prediction model of impairment

To answer the second research question of experiment A, which vestibular assessments are redundant in adult patients with CI or VS, a binary logistic regression was performed to see whether a combination of tests could predict the difference between the impaired and unimpaired patients. The analysis showed that using the forward method, the MSPV of both warm and cold calorics, the gain of the lateral canal and the functional score of the DHI could predict significantly which patients were impaired or unimpaired, $\chi^2(4)=469.063$, $p=.000$ (see table 11). The MSPV of the warm calorics contributed significantly to the prediction whether patients were considered impaired or unimpaired correctly, $b=-1.176$, Wald $\chi^2(1)=14.032$, $p=.000$, as did the MSPV of the cold calorics, $b=-1.813$, Wald $\chi^2(1)=15.044$, $p=.000$. Only the gain of the lateral duct significantly predicted in the vHIT, the difference between impaired and unimpaired patients, $b=-6.866$, Wald $\chi^2(1)=6.564$, $p=.010$. The functional score of the DHI also contributed significantly to the prediction whether patients were impaired or unimpaired, $b=-.215$, Wald $\chi^2(1)=6.897$, $p=.009$. The odd ratios (<1) indicated that the chance of a patient being impaired decreased when the MSPVs of the calorics, the lateral gain of the vHIT or the functional score of the DHI increased (see table 11 step 1).

In contradiction with former analysis, the model changed a little when the difference in patient group (CI- and VS-patients) was added, using the forward and backward method, $\chi^2(5)=475.105$, $p=.000$. Both MSVPs of the warm and cold calorics still significantly predicted the chance that a patient was considered impaired or unimpaired, respectively $b=-1.574$, Wald $\chi^2(1)=11.040$, $p=.001$ for the MSPV of warm calorics and $b=-2.348$, Wald $\chi^2(1)=12.166$, $p=.000$ for the MSPV of cold calorics (see table 11 step 2). The gain of the lateral canal predicted significantly whether patients were labelled impaired or unimpaired, b=,.6-797 Wald $\chi^2(1)=5.879$, $p=.015$, as did the functional score of the DHI, $b=-.256$, Wald $\chi^2(1)=7.621$, $p=.006$. The difference in patient group also added a significant contribution to the prediction whether a patient was considered impaired or unimpaired, $b=2.709$, Wald $\chi^2(1)=4.302$, $p=.038$. The odd ratios of the MSPVs of the calorics, the gain of the lateral canal and the functional score indicate that when these results increased, the chance that a patient would be considered impaired decreased (see table 11 step 2). However, the odd ratio of the difference in patient group indicated that when a patient had a VS, the chance that he would be considered impaired increased. This could indicate that there would be different models for VS and CI-patients. When the analysis was repeated for each patient group was found for the CI-patients, the model consisted of the MSPVs of both warm and cold calorics, and the emotional score of the DHI. The model of VS-patients consisted of both MSPVs of the calorics also, but instead of the emotional DHI score, the total score and the lateral vHIT gain were included in the model.

Table 11. Results of the binary logistic regression

	b (SE)		95% CI for Odds Ratio Lower	Odds ratio	Upper
Step 1					
Constant	20.607 (5.193)	**			
MSPV Warm calorics	-1.176 (.314)	**	.167	.167	.571
MSPV Cold calorics	-1.813 (.486)	**	.065	.065	.408
Gain lateral canal	-6.866 (2.680)	*	.000	.001	.199
Functional score DHI	-.215 (.082)	**	.687	.687	.947
Step 2					
Constant	24.104 (6.641)	**			
MSPV Warm calorics	-1.574 (.474)	**	.082	.207	.524
MSPV Cold calorics	-2.348 (.673)	**	.026	.096	.358
Gain lateral canal	-6.797 (2.803)	*	.000	.001	.272
Functional score DHI	-.256 (.093)	**	.646	.774	.928
Patient group	2.709 (1.306)	*	1.161	15.014	194.179

*=p<.05, **=p<.01

Video head impulse test results versus caloric results

In the predictive model both caloric results and vHIT gain of the lateral SCC were given as predictors of impairment. To compare agreement between these tests, the results were compared (see table 12). Numbers of patients were categorized by caloric categories (vertically) and deviant vHIT gains (horizontally). The results of both ears were described. More than 40% of the patients showed normal caloric and vHIT results in the ipsilateral ear, while 11.4% showed no response on both tests.

Table 12. Comparison vHIT gains and caloric categories of all patients (N=430)

Ear with VS or CI			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	24	1	12	16	4	2	24	49	132
		Hypo	3	0	0	2	0	0	0	0	5
		Normal	11	1	2	6	0	0	4	0	24
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	8	0	0	9	0	0	1	2	20
		Hypo	5	0	0	2	0	0	0	0	7
		Normal	33	2	1	14	0	1	0	0	51
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	2	0	0	0	0	0	0	2	4
		Hypo	0	0	1	2	0	0	0	0	3
		Normal	144	2	2	20	0	2	4	0	174
		Hyper	4	0	0	0	0	0	0	0	4
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	3	0	0	0	0	0	0	0	3
		Hyper	2	0	0	1	0	0	0	0	3
		Total	239	6	18	72	4	5	33	53	430

Contralateral ear											
			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	6	0	1	2	1	0	1	5	16
		Hypo	1	0	0	0	0	0	0	0	1
		Normal	5	0	0	1	0	1	0	0	7
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	7	1	0	3	1	0	0	0	12
		Hypo	2	0	0	0	0	0	0	0	2
		Normal	21	0	0	7	0	1	0	0	29
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	1	0	0	0	0	0	0	0	1
		Hypo	5	0	1	1	0	1	0	0	8
		Normal	215	7	1	76	0	4	8	4	315
		Hyper	14	0	1	1	0	0	0	0	16
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	3	0	0	1	0	0	0	0	4
		Hyper	5	0	0	3	0	0	0	0	8
		Total	285	8	4	95	2	7	9	9	419

A number of patients showed normal caloric results in combination with a deviant gain of the posterior SCC (N=34). In almost 20% of the patients, this deviant gain was also seen in the contralateral ear (N=83). In Appendix I, this table was split for the separate patient groups. The effect of posterior gain losses was less common in the CI-group: 3.6% showed deviant results in the affected ear (N=4) and 9.7% in the contralateral ear (N=10). The VS-group showed more deviant posterior gains: 9.4% in the affected ear (N=30) and 23.1% in the contralateral ear (N=73). To examine this impairment some more, the deviant posterior gains of the contralateral ear were combined with caloric and vHIT results of the ipsilateral ear (see table 13, N=83, CI:VS=10:73, M:F=50:33). This table showed that 50.6% of the patients that had contralateral loss of the posterior canal, also showed ipsilateral canal dysfunction on both calorics and vHIT (N=42). In most patients deviant gains were reported in all three SCCs (N=22) or in both lateral and posterior SCCs (N=10). There was also a group of patients that had normal caloric results combined with a deviant gain of the posterior SCC (N=20). These patients showed isolated bilateral posterior SCC dysfunction, while their caloric results and anterior and lateral SCC gains were normal. These patients with isolated bilateral loss of the posterior SCC were mostly VS-patients (90%, CI:VS=18:2).

Table 13. Comparison of the ipsilateral vHIT gains and caloric categories of patients with contralateral deviant posterior vHIT gain (N=81)

Ear with VS or CI											
			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	1	0	2	7	1	0	10	22	43
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	1	0	1	1	0	0	3	0	6
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	1	0	0	2	0	0	0	0	3
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	0	0	0	9	0	0	0	0	9
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	1	2	0	0	0	0	3
		Normal	4	0	0	11	0	1	1	0	17
		Hyper	0	0	0	0	0	0	0	0	0
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0	0
		Hyper	0	0	0	0	0	0	0	0	0
		Total	7	0	4	32	1	1	14	22	81

3.2 Experiment B: pre/post comparison of pediatric patients with a CI

The results of the second experiment are described in the same order as experiment A: demographics, pre analyses and analyses to answer the research questions.

3.2.1 Demographics

Between April 2013 and April 2017, a total of 98 assessments concerned 71 pediatric patients (see table 14) and 27 of them were tested pre and post CI-surgery. Cause of the hearing dysfunction was unknown in 30% of the cases, congenital in 66% and acquired in 4% of the children (N=27). Five of them had a unilateral CI on the right side, six children had one on the left side and sixteen had bilateral CIs at time of testing (9 of them were implanted simultaneously). This resulted in 43 implanted ears to analyse on vestibular results.

The percentage of children that had vestibular impairment in one or both ears post-operatively could not be determined due to the amount of missing data of vHIT and caloric results. The analyses for this question are described in Appendix II, so that they can be used in the future when more data is available. In this appendix is also described which analyses can be used to determine how many children had deviant results on which combination of vestibular tests. These analyses could not be run due to the same reason, the amount of missing data, and due to the small sample (N=27).

Table 14. Demographics of experiment B

Demographics		
$N_{measurements}$		98
$N_{children}$		71
Age@testing (*M±SD*)		2.8±2.1
Sex (M:F)		28:42
Results by group		
Vestibular function	Pre-CI	Post-CI
N	27	27
Age@implant (*M±SD*)	2.2±1.7	
Age@testing (*M±SD*)	1.9±1.5	3.5±1.9
Sex (M:F)	12:15	
Side (AD:AS:ADS)		5:6:16

Success rates of vestibular tests

Because of the amount of missing data, success rates were calculated to calculate percentages of cases in which the tests were conducted successfully. Success rates of all vestibular measurements (N=98) and both pre and post assessments (N=27) are given (see tables 15a-b).

Table 15a. Success rates of all pediatric CI assessments N=98

Children pre/post CI N=98, M=2;9y, SD=2;1y, R=0;4y-6;11y				
	VST	CAL	vHIT (H)	vHIT (V)
Performed	97	87	85	38
Failed	22	53	13	10
Successful	75	34	72	28
Success rate(%)	77.3	39.1	84.7	73.7

Table 15b. Success rates of test results pre and post assessments N=27

Children pre and post CI 0;7-7 years, N=27			
Pre CI (M=1;11y, SD=1;6y)			
	VST	CAL*	vHIT**
Performed	26	25	17
Failed	5	15	2
Successful	21	10	15
Success rate (%)	77.8	37.0	55.6
Post CI (M=3;5y, SD=1;10y)			
	VST	CAL*	vHIT**
Performed	26	11	25
Failed	2	1	1
Successful	24	10	24
Success rate (%)	88.9	37.0	88.9

* The success rate of calorics was based on having results on at least one temperature.
** The vHIT success rate was based on horizontal canals only and is influenced by the fact that the vHIT was introduced in 2014 clinically.

The success rate of the VST is similar among the pre measurement and all CI measurements (77%, see table 15a). The post measurement of VST has a higher success rate of 89% (see table 15b). The calorics resulted in equal success rates between the different measurements (37-39%). The vHIT conducted in at least half of the children useful results (pre measurement) to almost 90% in the post measurement. For all CI measurements is seen that in 74% both vertical and horizontal canals could be tested.

3.2.2 Pre/post comparison of vestibular results

To answer the first research question of experiment B, whether the pre and post measurements resulted in significant different vestibular responses, all parameters of the VST, calorics and vHIT were assessed. The means and standard deviations of all parameters were given per vestibular test (see table 16).

Table 16. Means and standard deviations of the pediatric sample (*M±SD*).

Vestibular test	Pre-CI	Post-CI
VST		
Velocity	64.66 ± 36.97	56.41 ± 23.35
Time constant	14.00 ± 5.48	13.47 ±6.75
Gesamtamplitude	852 ±520	763 ± 485
Caloric MSPVs		
Warm	15.50 ± 10.60	16.25 ± 6.08
Cold	17.73 ± 18.07	22.09 ± 15.46
vHIT gains		
Anterior SCC	.88 ± .08	.92 ± .10
Lateral SCC	.88 ± .16	.95 ± .09
Posterior SCC	.54 ± .37	.50 ± .10

Velocity Step Test

Most children had reliable VST results (N=21), which resulted in data of 32 implanted ears to analyse the velocity, time constant and gesamtamplitude (GA) on significant differences pre and post-CI. A dependent t-test showed that there was no significant difference for velocity results between the pre and post measurement, t(31)=1.236, *p*=.226 (see figure 15a). This was also found in the time constant, t(31)=.346, *p*=.732 (see figure 15b). This resulted in no significant difference for GA between the pre and post assessment, t(31)=.921, *p*=.364 (see figure 15c).

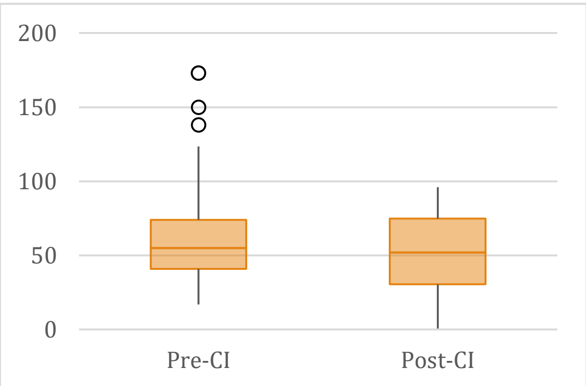


Figure 15a. Boxplot VST velocity – differences between pre and post-CI assessment. The pre-CI assessment had more distribution in the velocity results than post-CI, but the means did not differ significantly.

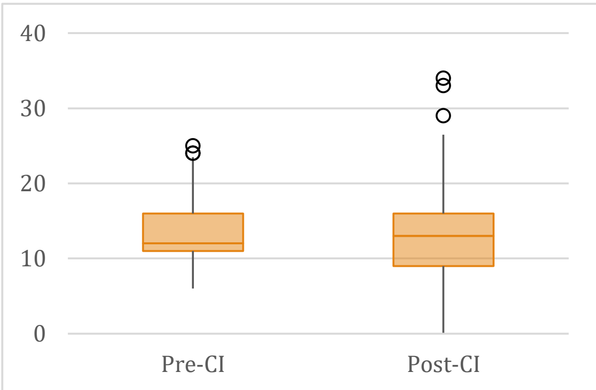


Figure 15b. Boxplot VST time constant – differences between pre and post-CI assessments. The means of both assessments did not differ significantly, although during the post-CI assessment the scores were more spread than during the pre-CI assessment.

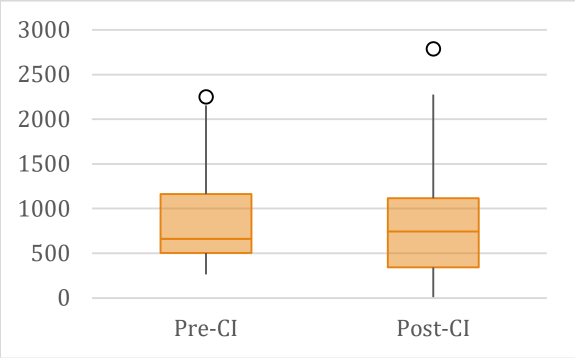


Figure 15c. Boxplot VST gesamtamplitude – differences between pre and post-CI assessments. During the assessment post-CI the GA results were more spread, but the means did not differ significantly.

Caloric testing

Only four children had reliable results for the warm calorics, which resulted in four ears to analyse the maximum slow phase velocity (MSPV) on significant differences pre and post-CI. A dependent t-test showed, no significant difference between the pre and the post assessment for the MSPV of the warm calorics, t(3)=-.092, *p*=.933. In addition to the continuous variable, a categorical variable for warm calorics was created. This variable was defined in four categories: areflexia, hyporeflexia, normal reflexia and hyperreflexia (see table 3 for values). The warm calorics$_{categorical}$ also revealed no significant difference between the pre and the post assessment, t(3)=-1.000, *p*=.391.

The cold calorics had more results to analyse than the warm calorics (see figure 16). This resulted in 11 implanted ears (N=10) to analyse the differences between pre and post-operatively. Between the pre and post assessments, no significant difference was found for the MSPV of the cold calorics, t(10)=-.640, *p*=.537. A categorical variable was also created for the cold calorics. The same four categories were defined: areflexia, hyporeflexia, normal reflexia and hyperreflexia (see table 3 for values). A dependent t-test showed that the cold calorics$_{categorical}$ did not significantly differed between the pre and the post measurement, t(10)=-2.055, *p*=.067.

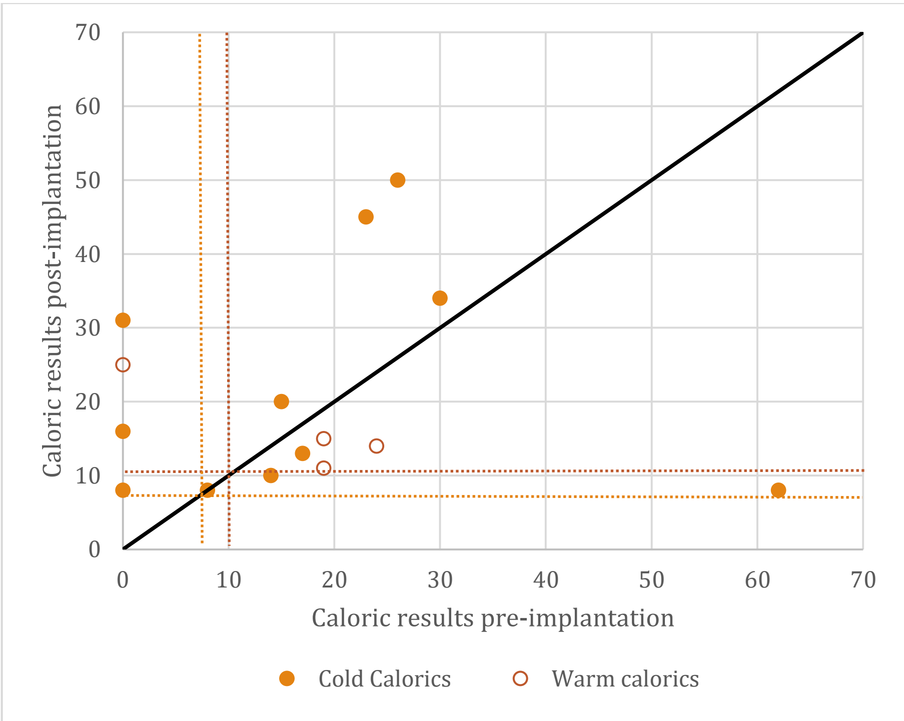


Figure 16. Scatterplot of the pre and post-CI caloric results. The black line defines the exact same results pre and post CI. The dotted lines represent the limits for normal or deviant caloric results. For cold calorics (orange) a large distribution is seen. Three ears had no response pre-CI, while they had normal responses post-operatively. One ear responded hyperreactive pre-CI and deteriorated to a normal response post-CI.

The warm calorics (red open) have less results. Three ears had normal responses both pre and post-CI, while one ear did not respond pre-CI and had a normal response post-CI.

Video Head Impulse Test

The anterior SCC had reliable gains of the vHIT for four children of the sample, which resulted in five implanted ears to analyse on pre and post-CI differences. A dependent t-test showed no significant difference in the gains of the anterior SCC between the pre and post assessments, t(4)=-.805, *p*=.466. The lateral SCC was measured more successfully with the vHIT than the anterior canal, which resulted in 22 implanted ears to analyse on pre and post-CI differences in 16 children (see figure 17). A dependent t-test showed that there was a significant difference between the gains of the pre and post measurement of the lateral SCC, t(21)=-2.296, *p*=.032. The posterior SCC was measured by the vHIT reliable in four children, which resulted in five implanted ears to analyse on pre and post-CI differences. The analysis showed that there was no significant difference in the gains of the posterior SCC between the pre and post measurement, t(4)=.826, *p*=.455.

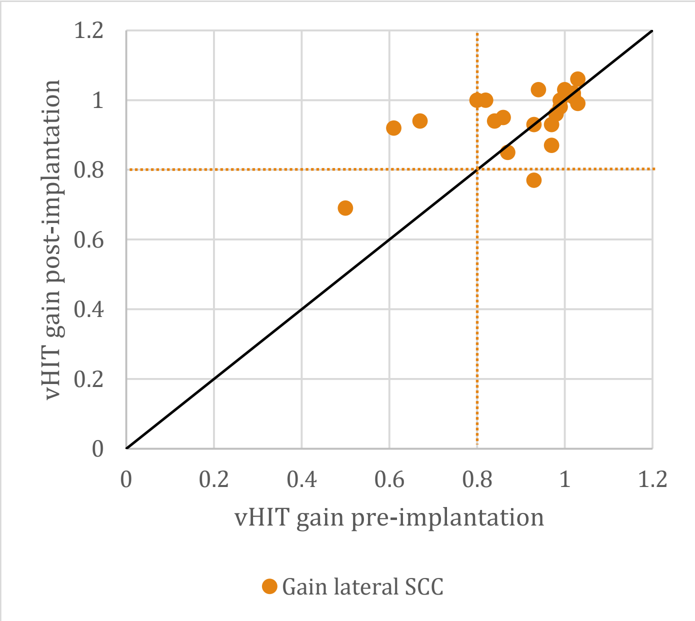


Figure 17. Scatterplot of the pre and post-CI vHIT gains of the lateral canal. The black line defines the exact same results pre and post-implantation. The orange dotted lines are the limits of normal or deviant results. The scatterplot shows that most implanted ears had normal gains on the vHIT for the lateral canal pre and post-CI. One ear had abnormal gains pre and post-CI, while two ears had better gains post-CI than pre-CI. Another ear had an abnormal gain post-CI, while it was normal pre-CI.

To answer the second research question, which results of the vestibular assessment are redundant for pediatric patients with pre and post-CI measurement, the regressions and correlations from experiment A should be performed. Due to the amount of data, this research question could not be answered. The analysis are described for future research in appendix II.

3.2.2 Adjustments for pediatric applications

After the analyses, new applications for the pediatric protocol could be considered. Toys and lights were transformed into useful applications for the vestibular tests and questionnaires were considered for implementation. Both adult and pediatric questionnaires were analysed for new ideas in the pediatric protocol. A literature search was done to assess which questionnaires were available. During this search, Pubmed and Wiley Online Library were explored with different combinations of terms. After reading the abstract, 10 questionnaires remained for potential implementation. This were 8 questionnaires for adult patients and 2 for pediatric patients. They are described separately for each age group.

Adult questionnaires

In the systematic review of Fong et al. (2015) the Dizziness Handicap Inventory (DHI), the Activities-specific Balance (ABC) scale, the Vertigo Symptom Scale-short form (VSS-SF) and the visual vertigo analogue scale (VVAS) were mentioned as most commonly cited instruments for people with balance problems. Next to these questionnaires, more subjective measurements are available such as the Falls Efficacy Scale-International (FES-I) or the Vestibular Activities and Participation questionnaire (VAP; Friscia et al., 2014). These and more are described briefly and considered for translation and implementation.

Dizziness Handicap Inventory

The most frequently used vestibular questionnaire is the Dizziness Handicap Inventory (DHI). As mentioned before, it is a self-reported, validated questionnaire, designed to identify functional, emotional and physical factors associated with dizziness and vertigo (Mutlu & Serbetcioglu, 2013). In the study of Ardiç, Tümkaya, Akdağ & Şenol (2016) the original DHI, the screening form and the short form of the DHI were compared in 2111 vestibular patients. The screening form consisted of 10 questions and could be answered in the original scale "No" (0 points), "Sometimes" (2 points) and "Yes" (4 points). This screening does not contain subscales and 40 is the maximum score. The short form of the DHI consisted of 13 questions and these are answered as "Yes" (0 points) or "No" (1 point). In this form of the DHI a higher score indicates a better vestibular function, while in the original and the screening DHI a lower score indicates this. All three forms of the DHI were considered highly reliable (Cronbach's alpha>.8), although a discussion was mentioned about which subscales should be used. They concluded that the total score should be used rather than the sub scores for interpretation (Ardiç et al., 2016).

Activities-specific and Balance Confidence Scale

A well-known questionnaire is the Activities-specific and Balance Confidence (ABC) scale. It is often used in elderly to measure the psychological effect of balance problems and falling (Hill, 2005). So it is not used specifically for patients with vestibular problems. It takes ten to twenty minutes to fill in and the sixteen items are scales from 0 to 100 where different activities are rated on fear of falling. The self-reported questionnaire was found reliable (r=.92) and valid (Hill, 2005). Also significant correlations were found between a Spanish translation of the ABC scale and the (sub) scores of the DHI (r=.61-.74; Montilla-Ibáñez et al., 2017).

Visual Vertigo Analogue Scale

A questionnaire comparable to the ABC scale, is the visual vertigo analogue scale (VVAS). It is a quick and easy questionnaire, which indicates subjective vestibular problems. Patients are asked to indicate the intensity of symptoms related to imbalance, vertigo and dizziness on continuous scales ranging from zero to ten. A higher number indicates a greater impact (Grigol et al., 2016). Nine scales are part of the VVAS, where different situations that possibly trigger vestibular symptoms are rated on intensity of these symptoms. The VVAS was found to be consistent and reliable (Cronbach's alpha=.94) in a sample of 102 subjects with varying vestibular problems (Dannenbaum, Chilingaryan & Fung, 2011). The correlations of the VVAS with the original DHI were assessed and varied between r=.54 in 91 patients in the study of Grigol et al. (2016) to r=.67 in the study of Dannenbaum et al. (2011).

Vertigo Symptom Scale – Short form

The original Vertigo Symptom Scale (VSS) consists of 36 items and asks questions about the frequency and severity of dizziness symptoms during the last year. It contains two sub scales of symptoms: vertigo-balance and autonomic anxiety (Wilhelmsen et al., 2008). A shortened version, the Vertigo Symptom Scale – short form (VSS-SF), is introduced in 2008. It contains fifteen items which are scored on a five-point scale. A sum of item scores gives an indication of the symptom severity (>12 is severe dizziness). The two sub scales remain in the short form. Both forms of the VSS are found reliable and valid (Wilhelmsen et al., 2008).

Falls Efficacy Scale International
The Falls Efficacy Scale International (FES-I) is a self-reported questionnaire, aimed at elderly at fall risk. It is an evaluation tool used four times during one year and it contains sixteen items that are scored on a four-point scale (Delbaere et al., 2010). A short form was also developed and this questionnaire contains only seven items. The reliability and validity of the FES-I are found to be good, although the questionnaire is more aimed at people who have higher fall risks. It could contain more demanding balance-related activities to avoid a floor effect (Delbaere et al., 2010). The cut-off scores of >23 for the original FES-I and >10 for the short form are valid (Delbaere et al., 2010).

Vestibular Activities and Participation questionnaire
The Vestibular Activities and Participation questionnaire (VAP) is a 34 item questionnaire based on the International Classification of Functioning, Disability and Health, in particular the Activities and Participation component (Alghwiri et al., 2012). Different activities are rated on a five-point scale to indicate the functioning problems due to vestibular symptoms. The VAP was found reliable and valid in 58 patients. In the study of Mueller et al. (2015) evidence is found for a short version of the VAP, where only two factors remained and eleven of the 34 items were used.

Hospital Anxiety and Depression Scale
The Hospital Anxiety and Depression Scale (HADS) is a self-reported questionnaire of fourteen items in two sub scales. It was created to inidicate anxiety and depression symptoms in patients with physical problems, so it is not just focused on vestibular problems (Piker et al., 2015). The two sub scales of the HADS are the HADS-A (anxiety) and HADS-D (depression), but these scales are debated in literature due to differences in factor loadings. The correlations of the HADS with the DHI are moderate to strong (*r*=.54-.90). The internal consistency and reliability of the HADS are proven in 97 subjects (Cronsbach's alpha>.8).

Neuropsychological Vertigo Inventory
A new perspective and way of assessing subjective vestibular problems are implemented in the new Neuropsychological Vertigo Inventory (Lacroix et al., 2016). It is a self-reported online questionnaire containing seven sub scales in 28 items used for both central and peripheral vestibular problems. The seven sub scales are space perception, time perception, attention, memory, emotion, vision, motor and distractor. Not all scales were internally consistent (five of seven had a Cronbach's alpha>.8), but this questionnaire focusses more on cognitive influences of vestibular symptoms than the DHI does. The overall internal consistency and reliability was found to be strong in 108 patients (Cronbach's alpha=.88).

Between the questionnaires, there are many little differences. However, the most used questionnaires like the DHI and the ABC scale, seem to be enhanced in new questionnaires like the VVAS and the VSS-SF. Other new questionnaires are based on modern structures or new scientific perspectives. The VAP follows the structure of the ICF, commonly used in the clinical setting. The NVI is an online questionnaire, which can be implemented easily in an e-health community. This questionnaire also focusses on the cognitive problems that can accompany vestibular problems. Little literature has written about this topic, but it could be explored more in the future.

Pediatric questionnaires
In contrast to all the adult questionnaires, the pediatric questionnaires are developed less. Only two questionnaires were found during the literature search that were created for vestibular problems specifically and they differ in self-reported or parent-reported forms.

Dizziness Handicap Inventory for patient caregivers
The Dizziness Handicap Inventory for patient caregivers (DHI-PC) is an informant-reported questionnaire developed by the Vanderbilt University School of Medicine, so that subjective problems of vestibular patients in the age of five to twelve could be assessed (McCaslin et al., 2015). It consists of 21 items that have to be answered the same as the original DHI: "No" (0 points), "Sometimes" (2 points) or "Yes" (4 points). The categories of the total score are: 0-16 no limitation, 17-26 mild limitation, 27-43 moderate limitation and >43 severe limitation of participation and activity. The

questionnaire is found to be reliable and internally consistent (Cronbach's alpha=.93). A note for this version is that it is informant-rated and this needs to be taken in consideration when the results are interpreted. The perceptions of the patient can be influenced by the empathy of the caregiver.

Pediatric Vestibular Symptom Questionnaire
The Pediatric Vestibular Symptom Questionnaire is a self-rated questionnaire to indicate the intensity of vestibular problems that children have. The items are rated on a four-point scale and are suited for children in the age of six to seventeen years old. The questionnaire was found to have good internal consistency (Cronbach's alpha=.88; Pavlou et al., 2016). It was recommended that, when children with vestibular problems are assessed, also behavioural and psychological symptoms and quality of life should be assessed. A significant relationship was found between the PVSQ and the self-rated Strengths and Difficulties Questionnaire (SDQ). This is a 25-item questionnaire that screens behavioural symptoms on five different scales. The informant-rated version is developed for children in the age of seven to ten years old and the self-rated version is developed for children in the age of eleven to sixteen years old (Goodman, Melizer & Bailey, 1998). In email contact with the first author of the PVSQ article, it was mentioned that she would recommend a pediatric health-related quality of life questionnaire instead of the SDQ in future publications.

The two questionnaires were translated for the pediatric population, see appendix III and IV. Both translations were considered for implementation. In consultation was decided to implement the DHI-PC. The reasoning behind this decision was that the DHI-PC could be used on its own and the PVSQ had to be combined with another questionnaire. Five caregivers filled in the DHI-PC in the period of February 2017 to August 2017. The average time to fill in the questionnaire was five to ten minutes, which was no problem due to the fact that the parents could fill in the form while the children were assessed. Difficulties in the list were not detected yet, so the DHI-PC was also implemented in the digital patient file.

Pediatric balance measurements
In addition to a vestibular questionnaire, a motor performance measurement can be used to screen the balance motor skills of young children. A pediatric version of the Berg Balance scale (PBBS) is available for school-aged children (aged five to fifteen years old) and contains fourteen items. The PBBS was found to be reliable (rs=.89-1.0), but no normative data are found yet (Franjoine, Gunther & Taylor, 2003). Another measurement that could be used is the Bruininks-Seretsky Test of Motor Proficiency, Second Edition (BOT-2). It assesses gross and fine motor skills of children aged four to 21 years (Deitz, Kartin & Kopp, 2007). This measurement is not only focussed on balance (like the PBBS), but also on other motor skills. It contains nine items that focus on balance, while the whole measurement contains 53 items and takes 40 minutes to one hour to complete (Deitz et al., 2007). So if only the balance items are used, no normative data is available. However, it could be useful to add some functional balance items in the pediatric protocol to screen for early functional deficiencies.

Applications for the vestibular assessment
The questionnaires and balance measurements could be implemented to indicate subjective vestibular problems. But to enhance the participation of children during the vestibular assessment, other adjustments had to be made. To make the saccade test more playful, a little house board was developed. The idea came from a clinician in Paris, who used such a house in the vestibular assessment with children. The first house was made of cardboard and its dimensions were calculated on the basis of the angles of the saccade test (windows were created at ten and twenty degrees horizontally and 10 degrees vertically). Little multi-coloured lights could be moved between the windows, so that a saccadic test was mimicked. The optokinetic test was also adjusted to the ideas of the Parisian clinician. A roller was created, with black and yellow stripes. The roller could be spun before the eyes of the child and a fast optokinetic test was mimicked. The video head impulse test was adjusted with multi-coloured lights placed on the dots. Because of the changing colours of the lights, the children were able to focus longer on the same point.

4. Discussion

This study tried to find evidence for a standard vestibular test protocol. The scientific evidence was inconclusive about which combination of vestibular tests had to be most preferred in clinical settings. The most optimal protocol would contain bithermal caloric testing, video head impulse testing (vHIT) and the Dizziness Handicap Index (DHI). These tests best predicted the difference between impaired and unimpaired patients. The VST could be a useful addition. In experiment A, this was investigated by assessing correlations within and between vestibular tests and their agreement with the DHI in a sample of patients with possible unilateral vestibular weakness (UVW). The correlations between tests were weak ($rs<.60$), so very little agreement between the tests was observed indicating that the tests measure different components of the vestibular system. A statistic prediction model that linked objective vestibular test results to the subjective DHI scores revealed a few predictors, which explained only little variance. This indicated little agreement between the DHI and other vestibular tests. In experiment B an optimal protocol was analysed for children aged under seven, but due to an amount of missing data and few subjects (N=27) these analyses did not lead to robust conclusions. Additionally, a comparison was made between vestibular results of pre and post-operative data of cochlear implanted (CI) children, but the results showed no significant pre-postop differences. This suggested a low risk of damage to the vestibular system when a child is implanted at an early age.

4.1 Experiment A: correlations in test results of adult patients with UVW

In this experiment, a prediction model was formed that indicated which patients were impaired and which were not. UVW of the impaired group was defined as areflexic results on both caloric tests and deviant vHIT gains of all three semicircular canals (SCCs). The following vestibular parameters were included in the model of impairment (model 3): MSPVs of both calorics, vHIT gain of the lateral semicircular SCC and functional score of the DHI. This model indicated that both calorics have to be kept in the protocol to differentiate better between impaired and unimpaired patients. In contrast to this statement, the strong correlation between both MSPVs could suggest that they measure the same and one temperature in the protocol would suffice. The meta-analysis of Adams et al. (2016) concluded that monothermal calorics lacks sensitivity, which agrees with the present model of keeping both temperatures in the caloric testing protocol. To conclude, for the overall protocol, the following vestibular tests are necessary for differentiation between impaired and unimpaired patients: the vHIT, bithermal calorics and the DHI. The vHIT could be limited to the assessment of only the lateral canals, while the functional score of the DHI seems most indicative for vestibular impairment.

4.1.1 Agreement between objective test results and the subjective DHI scores

The subjective DHI was included in the predictive model of impairment (model 3). The objective test results were linked to this subjective measurement in significant correlations. The DHI scores correlated negatively with parameters of the calorics, vHIT and VST. This indicated a normal relation between the parameters. However, these effects were only weak and were not clinically relevant. Predictive models of total DHI score (model 1) and categories (model 2) contained a combination of MSPV of cold calorics with posterior SCC gain of the vHIT or time constant of the VST. Both models explained just a small amount of variance, which questions the relevance of the models. Variables such as gender, age and difference in patient group, had their effect on the model and removed the posterior vHIT gain from model 1. These results agree with the weak correlations between the DHI and the objective tests. Therefore, it can be concluded that objective test results of the VST, vHIT and calorics do not agree with the subjective DHI score. This is in conformity with earlier findings in 30 CI-patients (Batuecas-Caletrio et al., 2015a) and in 49 VS-patients (Batuecas-Caletrio et al., 2013): they found that unilateral vestibular impairment resulted in higher DHI scores, although they still correlated poorly with objective test results.

The weak correlations might be explained by vestibular compensation abilities. The visual and proprioceptive signals adjust to the vestibular function within a couple of weeks (Sadeghi, Minor & Cullen, 2010). However, this only affects the low-frequency head movements (Eatock & Songer, 2011). Recent evidence states that in contrast to auditory hair cells, new vestibular sensory cells can develop during life or that these hair cells can be regenerated, but the compensation only applies to low-frequency dependent type II hair cells due to a lack of forming new calyceal afferent endings of type I hair cells and not to high-frequency impulsive head motions (Burns & Stone, 2017). It is still unknown why this does not happen for type I hair cells at this time. Despite of this incomplete compensation, the DHI might be not sensitive enough in detecting remaining vestibular problems of high-frequency head movements after compensation. This contradicts the moderate to strong correlations between the sub scores of the DHI. They indicated a linear relation between physical, functional and emotional scores. If compensation would arise effectively, the emotional score would be expected to be lower than the physical and functional scores. This is not seen in the data of this study and suggests that the DHI is not sensitive enough to detect compensation, although DHI scores do not agree with objective test results.

4.1.2 Redundancy between vestibular tests

The standard protocol in the Radboud University Medical Centre (RadboudUMC) contains vHIT, bithermal calorics, velocity step test (VST) and DHI. The preferred protocol of this study did not contain the VST. The question rises whether it still needs to be in the protocol. Analysis of this study showed that the VST differentiated correctly between the impaired and the unimpaired patients, as did all individual tests. However, no parameter of the VST was included in the prediction model. The same applied to the prediction model of the DHI score. This showed that the VST did not significantly add to the prediction models of determining objective or subjective vestibular problems. But is that the purpose of the VST? It is the only test that measures bilateral vestibular function. The test assesses the vestibular response of both ears on low-frequency stimuli. The test identifies residual vestibular function after acute vestibulopathy and monitors compensation of the vestibular system (Chan et al., 2016). The ability to monitor compensation was not seen in any of the other vestibular tests. So the VST still can contribute significantly to the vestibular assessment.

Another consideration for the protocol was determining whether the vHIT and calorics agreed on such level that they could be considered redundant. These tests correlated most between tests, although the effect sizes were still weak. This was in accordance with earlier findings (Blödow et al., 2015; Tranter-Entwistle et al.; 2016). Little agreement between the tests assessing the lateral SCC resulted also from the study of Eza-Nuñez et al. (2016). The same effect can be seen in this study, when MSPVs of calorics and vHIT gains were compared (see table 12): in this table patients are labelled on caloric categories and combinations of deviant vHIT gains. Both the affected ear and the contralateral ear were displayed in the table to assess agreement between the two tests. In the ipsilateral ear, various semicircular canals (SCCs) could show deviant vHIT gains when areflexic caloric results were found. This indicated agreement between the tests, because both tests show diminished vestibular responses. The agreement was also seen in the saturation point of the normal caloric results and the normal vHIT results. However, when an areflexic or hyporeflexic caloric result was found, the vHIT did not always show a deviant gain for the lateral duct. This contradicted agreement between the tests, because one test showed no lateral SCC response, whereas the other test did. This group of patients diminish the strength of the correlation and refute agreement between the tests. In former studies, the vHIT and calorics are seen as complementary instead of redundant (Blödow et al., 2015; Tranter-Entwistle et al., 2016). The data of this study was in conformity with that statement of Blödow et al. (2015) and Tranter-Entwistle et al. (2016) and retains both calorics and vHIT in the protocol.

The difference between the vHIT and caloric results could be due to a difference in frequency examination (Blödow et al., 2015). The difference might be explained by a frequency-dependent neural organization of regular firing and irregular firing afferents (Sadeghi et al., 2007). They reported that regular firing afferents had an effect on the vestibulo-ocular reflex (VOR) below frequencies of 4 Hz and that irregular firing afferents had effect on high-frequency head rotations (>4 Hz). Furthermore, the irregular firing afferents were found to be connected to sensory receptor cells (type I hair cells) in the central zone of the crista ampullaris of the SCCs, while the regular firing afferents were connected to type II hair cells in the peripheral zone of the crista ampullaris (Sadeghi et al., 2007). A type I hair cell has a myelinated afferent axon and is surrounded by a calyceal synapse, while a type II hair cell has an unmyelinated bouton afferent axon (Burns & Stone, 2017). In contrast, Eatock & Songer (2011) described that because of the morphological differences, a type I hair cell can process high-frequency head motions better than type II hair cells and that in all assessed mammals (humans included) the two afferent streams are connected to both types of hair cells in the central and peripheral zones of the cristae ampullaris. Only in birds and reptiles type I hair cells are solely found in central zones as described in Sadeghi et al. (2007). The review of Burns & Stone (2017) described that depending on the zone, the hair cells are different in structure of hair-bundle and synaptic specializations. The central zone contains larger and more complex type I and II hair cells, whereas the hair cells in the peripheral zones are more simple. The connecting neurons can be dimorphic to both axons, although neurons can be monomorphic too. Monomorphic type I hair cells only exist in central zones, while the monomorphic bouton neurons are found in the peripheral zones. However, the functional differences between these morphological features (type of hair cells, difference in afferents or neurons) is not clear yet. Additionally, the electrophysiological differences between the two streams and zones are not well understood. Another article stated that central zones and irregular afferents process high-frequency head movements better, whereas the peripheral zones are more prone to low-frequency head motions (Halmagyi et al., 2017). But the distinguishing features still need to be more assessed, since the frequency-dependency is not clear yet.

Isolated loss of the posterior canal

In table 12, 23% of the patients showed isolated loss of the posterior SCC. A remarkable note is that most deviant posterior gains were found in the contralateral ear (20%) instead of the ipsilateral ear (8%). This loss was mostly seen in VS-patients and to lesser extent in CI-patients, see Appendix I. This is in agreement with the study of Tarnutzer et al. (2017), who described that it is more common in VS-patients, although the contralateral damage cannot be explained yet. They observed an incidence of 2% in their patient population. The incidence of this study was biased by the amount of VS-patients.

It is not expected that the deviant gains were caused by artifacts of the posterior vHIT measurement, because head motion artifacts cause an increase of VOR gain, whereas an eyelid interference seldom appears in a posterior SCC vHIT movement (Halmagyi et al. 2017).

Most patients in this study had unilateral posterior loss: 3.3% in the ipsilateral ear and 14.7% in the contralateral ear. This last group is most interesting, because the ear that is affected by a CI or a VS showed normal vHIT gains and calorics, while a deviant vHIT gain for the posterior SCC was only found in the contralateral ear. The caloric and vHIT results of the ipsilateral ear of these patients are given (see table 13): half of the patients with contralateral posterior loss also showed a UVW in the ipsilateral ear.

An explanation of contralateral posterior loss is not known. In CI-patients, who have normal vestibular function, a contralateral loss is not expected, since surgical intervention is limited to only one side in these patients. VS-patients showed this isolated loss more often. However, a significant amount of patients in the dataset (N=20) also showed isolated *bilateral* loss of the posterior SCC. These twenty patients were 4.7% of the total sample measured by vHIT and calorics (N=430). The loss of these patients suggests that the posterior canal can be affected by an unknown origin and deteriorate independently. Evidence indicates that vHIT results can facilitate localizing the VS. In combination with an impaired cVEMP for instance, damage to the inferior branch of the vestibular nerve can be expected, while impaired caloric results indicate superior branch impairment (Day et al., 2009; Tarnutzer et al., 2017). This could indicate that the inferior branch of the vestibular nerve is damaged by an unknown cause. However, more research has to be done to explain this isolated posterior loss.

4.1.3 Effect of demographic factors on the models

The predictive model of impairment (model 3) was not affected by age or gender, whereas the difference in patient group did have its effect on the model. This was not expected due to the prior analysis investigating significant differences between VS and CI-patients. Since effect sizes appeared to be weak, it was concluded that patients did not differ significantly so that data could be pooled for further analysis. However, the model could indicate different vestibular protocols for the patient groups. Analysis of each patient group separately resulted in slightly different models. Both models contained the caloric MSPVs, but differed in DHI scores and the lateral vHIT gain. An explanation for the different outcomes between the analysis, is that the analysis itself could have influenced the effect of the patient groups. The prior analyses were straightforward t-tests, while the predictive models were composed in regressions. The effect of patient group could have been enlarged in these latter analyses. The model differences are only small though, and do not specifically indicate the need for different protocols.

The fact that age did not affect the model is remarkable considering the anatomical theory. As described before, renewal and regeneration of vestibular hair cells are possible, although not completely (Burns & Songer, 2017). It was observed that the type I and II hair cells degenerate in number due to aging. The vestibular ganglion neurons also appear to diminish in function during life. The degeneration seems to have a significant onset between the age of 65 and 70 years old was stated by Zalewski (2015).

To demonstrate this age-dependent vestibular degeneration using objective tests is a challenge, although it was observed in the data of the subjective DHI, because it was included as predictor in the predictive model of DHI scores (model 1). A former study where an age effect was found, is the study of Chan et al. (2015). They formed normative data for rotational chair testing for different age groups ranging from 6 to over 50 years old. The study showed that VOR gain decreased with age. In contrast, were in an earlier study of Maes et al. (2010) no significant age trends reported for both sinusoidal harmonic acceleration test and velocity step test parameters. Subtle decline was observed, but did not result in significant age differences. They also found the same effect for caloric testing. Only little diminishing MSPVs were observed, but this did not result in a significant age-dependency. This is in agreement with the vHIT results of Halmagyi et al. (2017) and the same conclusions were drawn by the normative study of McGarvie et al. (2015) who found no significant effect of age in the VOR gains measured by the vHIT, despite the fact that a decrease of gains was observed. The same effect was observed in the pediatric study of Ross & Helminski (2016), who concluded that the vHIT gains were not affected by age, although the pediatric subjects needed more trials to obtain a reliable calculation of the gain. However, in a recent study of Wiener-Vacher & Wiener (2017), normative values of vHIT gains for different ages were defined for infants and children: they observed a monotonical but irregular development of VOR gain until the age of six. Older children showed a more gradual development of VOR gain. The vHIT gain increased with age, but they did not define new cut-off levels for the vHIT, since the values were still within normal ranges. This non-appearing age effect in the vestibular tests contradicts the theory that type I hair cells process high-velocity head movements and that these cells are degenerating during life. The vHIT might not be sensitive enough to detect these age-related vestibular decline. So the fact that the model excluded age as predicting factor, does not agree with the underlying anatomical idea, but does agree with the observed results of the vestibular tests.

4.1.4 Limitations of experiment A

The sample of experiment A consisted of many patients and data, although data still was missing for an overall protocol. The sample contained only CI and VS-patients, but since the aim was to consider all patients with unilateral vestibular weakness, a larger group of more different patient groups could be included.

Due to the retrospective nature of this experiment, not all vestibular tests could be taken into consideration for the standard test battery. The RadboudUMC does not include ocular vestibular-evoked myogenic potential (oVEMP) or cervical vestibular-evoked myogenic potentials (cVEMP) testing to test otoliths. For this reason, the two otoliths of our vestibular organs were not tested, but only the three SCCs. Inclusion of VEMP data might have a significant contribution to the predictive models that were used, since in the present study unilateral vestibular weakness (UVW) was only defined as areflexic results on both caloric tests and deviant vHIT gains on all three SCCs, without taking into account the otolitic (utricle, saccule) functionality. Another definition based on all five vestibular organs, could have led to other distributions of the impaired and unimpaired group and other predictive models. The intra and interreliability of the test results were retained, because only two clinicians performed all measurements in the included period and the test results were revised by one clinical physicist.

In all analyses, the comparison between the impaired and the unimpaired group was made, but the patient groups were not compared to a healthy control group. Within groups, the unimpaired CI and VS-patients were considered as control group. However, this could have biased the models, because these patients were considered healthy, while they might have not been. From another perspective, solely the group with moderate to severe DHI scores could be analysed in another experiment. That specific patient group could show different predictive models, because this sample contained a lot of unimpaired patients.

4.2 Experiment B: pre/post comparison of pediatric patients with a CI

In the second experiment, data of pediatric CI-patients in the age of six months to seven years was assessed. Because of the concentration capabilities and instruction limitations in the pediatric vestibular assessment, only a few children were measured pre and post CI-surgery in the assessed period of May 2013 to April 2017. This could be due to the fact that in the RadboudUMC, parents can decline the request for a vestibular assessment post-CI. Only 27 of the 71 children were measured pre and post-CI. This is more than in the study of Thierry et al. (2015), where only 12 of 577 children were tested pre and post-CI.

4.2.1 Pre/post comparison of vestibular results

The vestibular results of the 27 pediatric patients measured pre and post-CI, were analysed on significant differences between the measurements. The analyses showed no significant differences pre and post-CI on all tests (the VST, vHIT and calorics) for patients in the age of six months to seven years old, except the vHIT gain of the lateral SCC. However, this difference contained an increase of vHIT gain and not a decrease of vHIT gain and thus vestibular function. This contradicts vestibular diminishment due to CI-surgery, but is probably biased by better trials. This evidence was in conformity with an earlier study of Ajalloueyan et al. (2017), which also did not report significant differences in 27 children in the age of one to four years old. The conclusion of the study of Stultiens (2017) also agrees with the results of this study. He concluded that cochlear implantation only led to small changes in vestibular function in 192 adult CI-patients. The meta-analyses of Ibrahim et al. (2017) stated that only calorics was negatively affected by CI of all vestibular tests. This trend was also seen in the study of Stultiens (2017), but did not result in a significant difference. The findings of this study showed increasing caloric responses, although this could be caused by better participation of the child. So it seems that cochlear implantation has no significant effect on vestibular function in children aged up to seven years old.

4.2.2 Redundancy in the protocol

Correlations and regressions could not be performed in the data of the pediatric patients, due to the amount of missing data and the small sample size. The test battery could not be statistically analysed as in experiment A. The failed analyses are described in Appendix II.

In addition to the failed analyses of the protocol, no percentage of vestibular dysfunction could be determined due to the fact that most measurements contained a lot of missing data. These analyses are also described in Appendix II. Instead of this, success rates of the vestibular tests were calculated. Most vestibular tests could be performed successful with pediatric patients, indicated the success rates. As expected due to their younger age, the rates were lower for the children during their first assessment (pre-CI) than their second (post-CI). However, the overall rates were still quite good. The VST and vHIT could be performed in approximately 75% of all pediatric patients. The vHIT contained both lateral and vertical SCCs. The calorics had the lowest success rate: it did not rise above 40%. These success rates confirmed that vestibular assessment was possible in most cases and needs to be tried in every CI-patient. Vestibular assessment is important for children pre and post-CI to keep track of vestibular changes as described in Jacot et al. (2009) and Cushing et al. (2013),

4.2.3 Adjustments for pediatric applications

Adjustments for the pediatric protocol were applied to increase success rates and participation of the pediatric patient more. Several questionnaires were considered for implementation, which resulted in the implantation of the DHI for patient caregivers (DHI-PC). The first impression of this questionnaire was positive and further implementation of this questionnaire will follow. Other adjustments for the vHIT and oculomotor tests were created and were also implemented in the pediatric protocol.

4.2.4 Limitations of experiment B

The limitations of this experiment were the amount of missing data and the small number of pediatric patients, so that the power of the analyses was low. This meant that most analyses were more indicative of trends, than that they could determine whether significant differences exist. Significant differences could have been found when more data was available, although literature suggested it would not, because no significant differences were found in CI-patients (Ajalloueyan et al., 2017). The small dataset also led to inability of answering the second research question. The analyses needed for that question, could not be run with so little data (see Appendix II).

In this experiment, results of the implanted ear were not compared to results of the non-implanted ear within subjects. Most children were implanted bilaterally, so this was not possible for every child. This could have affected the analyses in combination with an age effect. As described in the study of Wiener-Vacher & Wiener (2017), the VOR gain increases dependent on age. This age effect is not taken into account in this experiment.

In the adjustments for applications in the pediatric assessment, the DHI-PC was translated to Dutch. This was done by one author and this could have an effect on the translation. Differences in translation of feeling ‘down’ or feeling ‘unhappy’ were hard to display in Dutch.

5. Conclusion

This study contains several take home messages following the two different experiments concerning the velocity step test (VST), caloric tests, video head impulse test (vHIT) and the Dizziness Handicap Inventory (DHI).

5.1 Experiment A: correlations in test results of adult patients with UVW

- The results of the objective vestibular tests (VST, calorics and vHIT), correlated and predicted poorly the results of the subjective DHI.
- The protocol of vestibular assessment should contain the VST, bithermal calorics, vHIT and DHI due to the fact that all tests measure other components of the vestibular system.

5.2 Experiment B: pre/post comparison of pediatric patients with a CI

- The results differed not significantly between the pre and post-CI vestibular assessments in pediatric patients.
- The DHI for patient caregivers seems a useful addition to the pediatric vestibular protocol.

6. Recommendations

In line with the limitations of the experiment of this study and the unanswered research questions, recommendations for future research can be formed.

6.1 Experiment A: correlations in test results of adult patients with UVW

In this experiment, a standard test battery for the vestibular assessment for patients with a unilateral vestibular weakness (UVW) was examined. Redundant tests should be disregarded in the protocol. This study recommends a combination of video head impulse testing (vHIT), bithermal calorics, velocity step test (VST) and dizziness handicap inventory (DHI) to use in a clinical setting. However, due to the fact that the RadboudUMC only performs VST, calorics, vHIT and DHI in CI and VS-patients, other tests were not considered for the protocol. Future research can add the ocular vestibulo-evoked myogenic potential (oVEMP) and cervical vestibulo-evoked myogenic potential (cVEMP) tests to the comparison, so that all vestibular tests are considered in the test battery. Adding these tests, also makes it possible to redefine UVW and include all five organs instead of the three semicircular canals (SCCs). The UWV definition will be more complete then.

The sample can be adjusted by adding a healthy control group and more pathologies that result in chronic UVW. In addition the effect of different patient groups on the test battery can be assessed, to examine whether different protocols are necessary. This is recommended to take bias out of the analysis.

In the data of this study, the patients with isolated contralateral posterior loss measured by the vHIT were striking. This study recommends more research focussed on this phenomenon what seems to occur more in VS-patients. The origin and incidence is not clear yet.

6.2 Experiment B: pre/post comparison of pediatric patients with a CI

The main recommendation for this experiment, which compared vestibular results of pediatric patients pre and post-CI and whether redundant tests were used in the pediatric protocol, is that in future research a larger sample has to be analysed again to see whether the trends of this experiment still hold up. In a larger sample, the same analyses can be done, taken into consideration an age effect by comparing the implanted and the non-implanted ear. This is recommended, because literature described such an age effect and this can bias the analyses.

Recommendations for the pediatric protocol are that all tests should be performed, because most tests have high success rates. Furthermore, testing should be applied before and after a CI-operation. Monitoring for vestibular impairment is important, because it can result in delayed motor development (Inoue et al., 2013).

The Dizziness Handicap Inventory for patient caregivers (DHI-PC) can be assessed more. Only one article introduced this questionnaire and this study tried to translate the DHI-PC to Dutch. This study recommends a normative validation study of the questionnaire, before this questionnaire can be integrated.

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Appendix I: Tables of vHIT gains versus caloric categories

In the chapter of results, tables of the whole sample are given. In this appendix the tables of the separate patients groups are displayed. First the CI-group (N=112 for the ipsilateral ear and N=103 for contralateral) and next the VS-group (N=318 for ipsilateral ear and N=316 for contralateral).

Table 17. Comparison of the vHIT gains and the caloric categories of the CI-patients

Ear with CI											
			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	8	0	0	2	0	1	3	5	19
		Hypo	2	0	0	0	0	0	0	0	2
		Normal	3	0	0	1	0	0	1	0	5
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	1	0	0	1	0	0	1	2	5
		Hypo	2	0	0	1	0	0	0	0	3
		Normal	10	0	1	0	0	1	0	0	12
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	1	0	0	0	0	0	0	1	2
		Hypo	0	0	0	1	0	0	0	0	1
		Normal	53	1	0	4	0	0	0	0	58
		Hyper	2	0	0	0	0	0	0	0	2
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	2	0	0	0	0	0	0	0	2
		Hyper	1	0	0	0	0	0	0	0	1
		Total	85	1	1	10	0	2	5	8	112
Contralateral ear											
			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	2	0	0	2	1	0	0	1	6
		Hypo	1	0	0	0	0	0	0	0	1
		Normal	2	0	0	1	0	0	0	0	3
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	1	0	0	1	1	0	0	0	3
		Hypo	1	0	0	0	0	0	0	0	1
		Normal	7	0	0	2	0	0	0	0	9
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	1	0	0	0	0	0	0	0	1
		Hypo	4	0	0	0	0	0	0	0	4
		Normal	55	4	0	8	0	1	2	2	72
		Hyper	0	0	0	0	0	0	0	0	0
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	1	0	0	1	0	0	0	0	2
		Hyper	1	0	0	0	0	0	0	0	1
		Total	76	4	0	15	2	1	2	3	103

Table 18. Comparison of the vHIT gains and the caloric categories of the VS-patients

Ear with VS

			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	16	1	12	14	4	1	21	44	113
		Hypo	1	0	0	2	0	0	0	0	3
		Normal	8	1	2	5	0	0	3	0	19
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	7	0	0	8	0	0	0	0	15
		Hypo	3	0	0	1	0	0	0	0	4
		Normal	23	2	0	14	0	0	0	0	39
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	1	0	0	0	0	0	0	1	2
		Hypo	0	0	1	1	0	0	0	0	2
		Normal	91	1	2	16	0	2	4	0	116
		Hyper	2	0	0	0	0	0	0	0	2
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	1	0	0	0	0	0	0	0	1
		Hyper	1	0	0	1	0	0	0	0	2
		Total	154	5	17	62	4	3	28	45	318

Contralateral ear

			vHIT (deviant gains)								
	Warm	Cold	Normal	A	L	P	A+L	A+P	L+P	A+L+P	Total
Calorics (categories)	A	A	4	0	1	0	0	0	1	4	10
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	3	0	0	0	0	1	0	0	4
		Hyper	0	0	0	0	0	0	0	0	0
	Hypo	A	6	1	0	2	0	0	0	0	9
		Hypo	1	0	0	0	0	0	0	0	1
		Normal	14	0	0	5	0	1	0	0	20
		Hyper	0	0	0	0	0	0	0	0	0
	Normal	A	0	0	0	0	0	0	0	0	0
		Hypo	1	0	1	1	0	1	0	0	4
		Normal	160	3	1	68	0	3	6	2	243
		Hyper	14	0	1	1	0	0	0	0	16
	Hyper	A	0	0	0	0	0	0	0	0	0
		Hypo	0	0	0	0	0	0	0	0	0
		Normal	2	0	0	0	0	0	0	0	2
		Hyper	4	0	0	3	0	0	0	0	7
		Total	209	4	4	80	0	6	7	6	316

Appendix II: failed analyses of experiment B

Not all analyses could be run to answer the research questions. Due to the small number of children measured pre- and post-CI, the analyses failed to run. The analyses are described in this appendix, so that they can be used in future research.

Percentage impaired vestibular ears post-operatively

In experiment A, an impaired group was formed due to deviant results on the calorics and vHIT. Due to the amount of missing data in experiment B, the same comparison could not be made for the children. The used analyses are described here, so that they can be used in the future.

The RECODE command can be used to create categorical variables for the vHIT and calorics. The vHIT gains can seperately be recoded in dichotomous variable 'normal'/'deviant' and calorics in different categories such as 'areflexia'/'hyporeflexia'/'normal reflexia'/'hyperreflexia'. In a crosstab analysis, caloric labels can be shown combined with the deviant vHIT gains. The children with areflexic results on calorics and deviant results on the vHIT can be considered as having an impaired vestibular system post-operatively.

Deviant results on a combination of vestibular tests

To determine how many children had deviant results on one or more vestibular tests, categorical variables were created for the vHIT, calorics and VST. Due to the amount of missing data and the small sample size (N=27), a fair comparison could not be made. The following analyses can be used to make the comparison in the future, when more data is available.

Through RECODE commands, categorical variables can be coded to transform the variables of the vestibular tests into categories such as 'normal'/'deviant' for vHIT or 'areflexia'/'hyporeflexia'/'normal reflexia'/'hyperreflexia' for calorics. A COMPUTE command can form one variable per vestibular test. A new COMPUTE command forms a variable that describes the results of every test pre-operatively and a variable that does the same post-operatively. Interpretation of the numbers given to categories of the variables is important (e.g. 5 means deviant results of the vHIT, 55 means deviant results for the vHIT and calorics and 555 means deviant results for all three tests). If descriptive analyses are run, a table can be formed where numbers or percentages describe how many children had deviant results on which combination of tests.

Appendix III: translation of the DHI-PC

Naam: Datum:

DIZZINESS HANDICAP INVENTORY VOOR KINDEREN – OUDERS/VERZORGERS
NEDERLANDSE VERTALING
(Leeftijd 5-12 jaar)

Instructie: Het doel van deze vragenlijst is om de moeilijkheden in kaart te brengen die uw kind mogelijk kan ervaren door zijn/haar duizeligheid of balansproblemen. Beantwoord elke vraag alstublieft met 'altijd', 'soms', of 'nooit'. **Beantwoord iedere vraag enkel met betrekking tot de duizeligheidsproblemen van uw kind.**

	Altijd	Soms	Nooit
1. Maakt het probleem van uw kind hem/haar moe?			
2. Wordt het leven van uw kind beheerst door het probleem?			
3. Is het moeilijk voor het kind om te spelen door het probleem?			
4. Is uw kind gefrustreerd door het probleem?			
5. Is uw kind in verlegenheid gebracht door het probleem in het bijzijn van anderen?			
6. Kan uw kind zich moeilijk concentreren door het probleem?			
7. Is uw kind gespannen door het probleem?			
8. Lijken andere personen geïrriteerd door het probleem van uw kind?			
9. Maakt uw kind zich zorgen door het probleem?			
10. Voelt uw kind zich boos door het probleem?			
11. Voelt uw kind zich 'down' door het probleem?			
12. Voelt uw kind zich ongelukkig door het probleem?			
13. Voelt uw kind zich anders dan andere kinderen door het probleem?			
14. Beperkt het probleem van uw kind zijn/haar deelname in sociale of educatieve activiteiten significant? Zoals het samen eten, vrienden ontmoeten, schoolreizen of naar feestjes gaan.			
15. Is het moeilijk voor uw kind om in het donker door het huis te lopen door het probleem?			
16. Heeft uw kind moeite met traplopen door het probleem?			
17. Heeft uw kind moeite om 400 meter te lopen door het probleem?			
18. Heeft uw kind moeite om te fietsen door het probleem?			
19. Is het moeilijk voor uw kind om te lezen of huiswerk te doen door het probleem?			
20. Is het moeilijk voor uw kind om bepaalde activiteiten succesvol uit te voeren in vergelijking met leeftijdsgenoten?			
21. Heeft uw kind moeite om zich te concentreren op school door het probleem?			

Appendix IV: translation of the PVSQ

Naam: Datum:

De Vestibulaire Symptoomvragenlijst voor Kinderen
Nederlandse vertaling van de PVSQ
(Leeftijd 6-17 jaar)

De volgende vragen gaan over hoe vaak jij je duizelig of wankel voelt. Kruis aan welk antwoord het beste bij je past.

Hoe vaak heb je dit ervaren in de afgelopen maand?

1. Een gevoel dat de wereld om je heen draait

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

2. Je voelt je zo wankel dat je echt valt

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

3. Een misselijk gevoel

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

4. Een licht gevoel in het hoofd

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

5. Het voelen van druk op je oren

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

6. Het niet scherp kunnen zien of stipjes zien

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

7. Hoofdpijn of druk in het hoofd voelen

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

8. Je kan niet staan of lopen zonder iets of iemand vast te houden

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

9. Je wankel voelen alsof je bijna gaat vallen

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

10. Een duizelig of vol gevoel in het hoofd

1 Heel vaak	2 Soms	3 Af en toe	4 Nooit	? Weet ik niet

11. Zorgen deze gevoelens ervoor dat jij stopt met dingen doen, die je graag zou willen doen? En zo ja, welke dingen?